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Pathology

EXPERIMENTAL PATHOLOGY

822. **Cardiac Lesions in Rabbits after Pharyngeal Infections with Group A Streptococci**

S. I. MORSE, J. E. DARNELL, W. A. THOMAS, and R. J. GLASER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] 89, 613–616, Aug.–Sept., 1955. 2 figs., 11 refs.

In their studies of the pathogenesis of rheumatic fever carried out at Washington University School of Medicine, St. Louis, the authors have developed a technique for producing pharyngeal infections in rabbits by intrapharyngeal inoculation with Group-A haemolytic streptococci, thus achieving conditions which are thought to simulate those occurring in man and from which rheumatic fever and cardiac lesions could ensue. Of 35 rabbits infected with various strains of streptococci, 27 showed histopathological cardiac lesions, characterized by muscle necrosis, cellular infiltration with mononuclear cells and Anitschkow myocytes, and disruption of collagen. After multiple infections and those of longer duration fibrosis occurred and giant cells were observed. No valvular changes were noted. Identification of the lesions as Aschoff nodules was not warranted; the authors suggest that this single difference from the appearances in rheumatic fever may be attributable to a variation in species reactivity. Blood and tissue cultures were all consistently negative. The pathological lesions were observed in 9 out of 12 rabbits as early as 2 days after inoculation. Three control groups totalling 62 animals were free of any such lesions, with a single exception in which one small area of necrotic muscle was observed. In the authors' opinion the appearance of these myocardial lesions within 24 hours of intrapharyngeal infection suggests that a non-immunological mechanism is involved.

Harry Coke

823. **Pathogenesis of Fatty and Sclerotic Lesions in the Cardiovascular System of Choline-deficient Rats**

G. F. WILGRAM and W. S. HARTROFT. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] 36, 298–305, June, 1955. 12 figs., 27 refs.

A study carried out at the University of Toronto showed that young rats fed on diets severely deficient in choline developed acute lesions in the heart and vessels within relatively short periods, microscopic deposits of stainable fat being observed in the aorta and coronary vessels as early as the 8th day; gross aortic sclerosis was observed from the 17th day onwards. In the coronary arteries the fatty change began in the intimal endothelial cells but later appeared in all layers of the arterial wall. The animals often died of cardiac or renal cortical necrosis before the lesions in the coronary arteries had progressed beyond this stage. Abundant deposits of stainable fat were demonstrated in the cardiac muscle cells in a high percentage of the animals, these cells subsequently becoming swollen and necrotic. There was a polymorphonuclear reaction to this necrotic process, followed later by round-cell infiltration and fibroblastic reaction. In the aorta the fatty change occurred in the intima in the early stages, being followed by degeneration and necrosis in the media and the eventual deposition of calcium salts, but there was little or no inflammatory reaction. Intimal fibrosis sometimes developed in the late stages. On the other hand, older animals receiving diets less severely deficient in choline developed chronic lesions which, however, did not appear before 3 to 4 months. In the coronary arteries of these rats lipid was deposited in the intima and media, small plaques being formed which sometimes encroached on the lumen. Focal areas of myocardial fibrosis also commonly appeared, but fatty deposits were rarely encountered. In the aorta the changes were similar to those of the late stages of the acute lesions. In the media bars of calcification were formed, while in the most advanced cases the entire thoracic aorta was converted into a rigid, dilated pipe.

Histochemical tests of the lipid in the acute lesions were positive for neutral fat and fatty acids but negative for phospholipid, cholesterol, and cholesterol esters. Periodic-acid–Schiff staining revealed intercellular deposition of mucopolysaccharides in the form of diffuse plaques and subendothelial nodules in the aorta and coronary arteries, while there was hyperplasia in the inner layer of these vessels; but no increase of mucopolysaccharides was found in the necrotic areas of the cardiac muscle. There was a positive haemosiderin reaction throughout the entire wall of the coronary arteries in some cases, and within the inner layer of the aorta of animals in both acute and chronic experiments. Iron pigment often appeared in granular form within the cardiac muscle fibres. Female rats were very resistant to the induction of cardiovascular and renal lesions, but the changes described above could be induced in 80% of females by the simultaneous administration of androgens and growth hormone.

The choline-deficient diets used in these experiments were relatively free of cholesterol. The addition of

cholesterol supplements to the choline-deficient diets of female rats and older male rats—which were otherwise resistant to the induction of cardiovasculo-renal lesions—induced such lesions in 75% of these animals. The addition of cholesterol to choline-supplemented diets had no ill effects, in spite of the fact that serum cholesterol levels were higher in rats given choline-supplemented diets than in choline-deficient animals, whether or not cholesterol was added to the diet. Thus dietary cholesterol aggravated the effects of choline deficiency on the cardiovasculo-renal system without producing an elevation of serum cholesterol levels. The authors conclude that the cardiovascular lesions were initiated by the deposition of fat as a result of the hypolipotropic diet, as in the case of hepatic and renal lesions. It appeared that the lesions in the myocardium and coronary arteries were directly due to the choline deficiency, whereas there was evidence that the aortic lesions might have been due, at least in part, to renal damage, which possibly induced secondary hyperparathyroidism and hence metastatic calcification.

Robert de Mowbray

824. **Influence of Gonadal Hormones on Protein–Lipid Relationships in Human Plasma**
E. M. Russ, H. A. Eder, and D. P. Barr. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 4–24, July, 1955. 2 figs., 26 refs.

Earlier studies reported by the authors from New York Hospital–Cornell Medical Center, New York (*Amer. J. Med.*, 1951, **11**, 468) have emphasized the influence of sex on protein–lipid relationships in human plasma. Results of further investigations are now reported.

To test the effects of oestrogens, " estinyl " (ethinyl oestradiol) was given to 7 male survivors of myocardial infarction for periods up to 6 months, it having been observed that in such patients there were usually abnormalities of plasma-protein–lipid patterns to a degree that should facilitate detection of any corrective action of the hormone. Plasma proteins were separated by method No. 10 of Cohn *et al.* (*J. Amer. chem. Soc.*, 1950, **72**, 465), in which alpha lipoproteins are recovered in Fraction IV+V+VI and beta lipoproteins in Fraction I+III. Analyses for protein, cholesterol, and phospholipids were made from these two lipoprotein fractions as well as from whole plasma.

Before treatment the percentage of cholesterol was lower than normal in alpha lipoprotein and higher than normal in beta lipoprotein, and the total cholesterol/phospholipid (C/P) ratio tended to be higher than normal both in whole plasma and in beta lipoprotein. The administration of 1 mg. of ethinyl oestradiol daily partially or completely reversed these changes, the maximum effect being obtained after about 6 weeks. There was no consistent effect upon anginal symptoms. Feminizing changes were induced. Nausea and vomiting occurred in some cases, but subsided in spite of continuing therapy. Similar effects were obtained with administration of " premarin " (oestrone sulphate), 15 mg. daily, to 8 survivors of cardiac infarction; of diethylstilboestrol, 36 mg. over 8 days, to 3 similar patients; and of oestradiol benzoate, 1·66 mg. daily, to a patient without evidence of atherosclerosis.

Administration of 1 mg. of ethinyl oestradiol daily to 6 patients with primary hypercholesterolaemic xanthomatosis (4 of whom had evidence of coronary sclerosis) led to a tendency towards a reduced concentration of cholesterol in whole plasma and in beta lipoprotein, and, as in the cases of cardiac infarction, a relative increase in alpha-lipoprotein cholesterol and a reduced C/P ratio in whole plasma and beta lipoprotein. In only one case was there any effect upon xanthomatous deposits, these almost disappearing. Administration of methyl testosterone, 50 mg. daily, to healthy subjects and to patients with various diseases invariably produced effects opposite to those of oestrogens. In fact protein–lipid patterns similar to those of atherosclerosis were induced in normal subjects, and those already present in atherosclerotic patients were enhanced. Administration of 1 mg. ethinyl oestradiol daily to 2 patients who were already receiving 50 mg. methyl testosterone daily did not modify the effect of the androgenic therapy, but the addition of 50 mg. methyl testosterone daily in 2 patients already receiving 1 mg. ethinyl oestradiol daily counteracted the effects of the oestrogen. Thus the effect of androgens was more potent than that of oestrogens. Moreover the effects of androgen given during or after oestrogen therapy were greater than those of androgen alone.

The authors suggest that their observations, like those of other workers, may provide a chemical basis for the relative immunity of young women to the complications of atherosclerosis. The therapeutic implications are less certain, especially in view of the side-effects of oestrogen therapy.

Robert de Mowbray

825. **A Study of Neural Factors in the Development of Febrile Reactions** (Материалы к изучению нервных механизмов лихорадочной реакции)
K. A. Pimenova. *Архив Патологии* [*Arkh. Patol.*] 17, 3–8, July–Sept., 1955. 4 figs., 5 refs.

In this study, which was carried out at the Leningrad Tuberculosis Institute, the author set out " to prove the decisive role of the nervous system in the development of a febrile reaction ".

In a series of 81 experiments on 27 rabbits fever was induced by the intravenous injection of a vaccine of *Bacillus mesentericus* in a dose of 1 ml. per kg. body weight. Each animal was subjected to three experiments at intervals of 3 to 4 weeks, preliminary investigations having established that at such intervals the febrile response is not influenced by previous vaccinations. Either just before injection of the vaccine or subsequently, an amount of air varying from 50 to 200 ml. was introduced into the peritoneal cavity. The author claims to have previously established that an artificial pneumoperitoneum " has a non-specific normalizing influence, similar to that of a procaine block, on the nervous regulation of the blood circulation and respiration ". Thus any alteration in the pattern of the febrile response to the vaccine following the induction of pneumoperitoneum was taken as evidence for the nervous origin of such response.

The induction of pneumoperitoneum 40 minutes before the injection of the vaccine was found to have a depressing effect on the febrile reaction which varied with the amount of air introduced. Induction of pneumoperitoneum from 1½ to 2½ hours after the injection, that is, at the height of pyrexia, produced a rapid fall of temperature which varied directly with the volume of air introduced, thus partially or completely abolishing the febrile response. *A. Swan*

826. **Different Reactions of the Organism to Intra-arterial and Intravenous Injections of Bile.** (Различная реакция организма при внутриартериальном и внутривенном введении желчи)
E. L. RABINOVICH. *Архив Патологии* [*Arkh. Patol.*] 17, 62, July–Sept., 1955.

The author describes experiments carried out at Minsk Medical Institute in which intra-arterial and intravenous injections of 0·3 to 0·5 ml. of bile per kg. body weight were given to 20 dogs. The bile used was heterogenous (ox bile), homogenous (bile from another dog), or autogenous (from the experimental dog itself); homogenous bile was found to be the most toxic of the three.

The intra-arterial injection of bile was followed by a stormy reaction, the animal "struggled, screamed, and soon became dyspnoeic", and the blood pressure rose by 20 to 70 mm. Hg. The duration of the reaction varied widely from animal to animal. In contrast, after the intravenous injection of bile in similar quantities the animal remained still, there was no dyspnoea, and the blood pressure fell. A preliminary infusion of procaine into the artery abolished or reduced the reaction to bile, but a similar infusion into the vein had no effect on the reaction to the intravenous injection of bile. When bile was introduced into the clamped end of the external jugular vein, and thus did not pass into the general circulation, the depressor reaction still took place.

The author concludes that these experiments prove the participation of a local reflex mechanism in the production of the reaction to the injection of bile.

A. Swan

CHEMICAL PATHOLOGY

827. **Serum Glutamic Oxalacetic Transaminase Activity as an Index of Liver Cell Injury: a Preliminary Report**
F. WRÓBLEWSKI and J. S. LADUE. *Annals of Internal Medicine* [*Ann. intern. Med.*] 43, 345–360, Aug., 1955. 14 figs., 5 refs.

Glutamic oxalacetic transaminase (G.O.T.) is widely distributed in animal tissues, its greatest concentration being in heart muscle, skeletal muscle, brain, liver, and kidney, decreasing in that order; it is also present in all types of human serum. At the Sloan-Kettering Institute and the Memorial Center for Cancer and Allied Diseases, New York, the authors found that the serum G.O.T. level in 500 normal adult individuals ranged from 5 to 40 units, with a mean of 22·1±6·8 units (one unit representing a change in optical density of 0·001 per ml. per minute at wave lengths of 340 μ). Further studies following myocardial infarction indicated that the enzyme was liberated into the blood stream following injury to cardiac muscle cells. From this the authors argued that if the enzyme is also released from damaged liver cells, the serum G.O.T. level should provide an index of the degree of liver-cell destruction, and the level and persistence of increased G.O.T. activity might then provide an index of active liver-cell disease. They have shown that this activity is not increased in patients with infectious, neoplastic, degenerative, metastatic, reactive, allergic, or congenital disease states unless there is also acute damage to liver tissue, heart muscle, or skeletal muscle.

In the present paper they report the variation in serum G.O.T. activity following acute liver-cell destruction, such as that seen after carbon tetrachloride poisoning in man (2 patients), and also during the course of acute infective hepatitis and homologous serum jaundice (10 cases), and compare the levels noted in these disorders with those in 28 patients with cirrhosis of varying degree, 5 with obstructive jaundice, and 22 with metastatic carcinoma of the liver. G.O.T. activity was determined spectrophotometrically immediately or on serum stored for periods up to 7 days at 0° C., and most of the usual liver function tests were also carried out. They found that serum G.O.T. activity was impressively increased following acute liver-cell injury due to carbon tetrachloride poisoning, the levels being 27,840 and 12,340 units respectively in the 2 patients 48 hours after exposure. In the patients with infective hepatitis or homologous serum hepatitis it was also elevated, to a maximum of 2,140 units. The serum G.O.T. activity in patients with acute liver cell damage was usually many times that seen in obstructive jaundice. Cirrhosis of the liver, however, may be associated with normal, mildly elevated, or high G.O.T. activity. This activity appears to be an index of the degree of liver-cell injury and does not necessarily correlate with hepatic dysfunction as shown by liver function tests. The increase in G.O.T. activity seems to be a relatively sensitive index of the extent of liver metastases, being an indicator of liver-cell destruction and not of liver function. *E. Forrai*

828. **An Evaluation of the Serum Iron in Liver Disease**
C. M. STONE, J. M. RUMBALL, and C. P. HASSETT. *Annals of Internal Medicine* [*Ann. intern. Med.*] 43, 229–240, Aug. 1955. 6 figs., 12 refs.

In reporting the serum iron levels as observed in one female and 60 male patients with liver disease admitted to the Veterans Administration Hospital, Coral Gables, Florida, the authors state that the determination of this value may be helpful in the differential diagnosis of hepatic disease with jaundice, since the liver plays an important role in the internal distribution of iron in the body. Some of the earlier Continental literature is reviewed.

In 25 healthy male subjects aged 21 to 63 years who acted as a control group the serum iron level ranged from 70 to 170 (mean 108·4) μg. per 100 ml. Of the 61 patients, in 56 of whom the diagnosis was confirmed by liver biopsy and in 5 at operation or necropsy, 17

were suffering from acute viral hepatitis, 34 from portal cirrhosis, and 10 from obstructive jaundice. In the majority of those with portal cirrhosis the serum iron level was found to be within the normal range. It was thought that the occasional extremely low serum iron levels found were consistent with the occurrence of gastro-intestinal bleeding; the suggestion that high serum iron levels are indicative of parenchymal cell necrosis could not be confirmed. In the group of 17 patients with acute hepatitis the serum iron level was high, ranging from 150 to 390 μg. per 100 ml., with a mean of 240 μg. per 100 ml. The cause for the elevation of the serum iron content in acute hepatitis is as yet unknown: the iron may be released during destruction of liver cells, or the inability of a damaged liver to store iron may be a factor. (The authors refer to 2 cases not included in this series in which cirrhosis was diagnosed until a raised serum iron level of 195 μg. per 100 ml. was found; in these cases liver biopsy examination later revealed the presence of haemosiderosis.) Patients with obstructive jaundice showed a serum iron level within the normal range (mean 116 μg. per 100 ml.), but nevertheless the determination is helpful in such cases in differentiating the condition from acute viral hepatitis. In the authors' experience the late appearance of the maximum rise in the serum iron level in acute hepatitis is suggestive of a more prolonged clinical course; it is possible that the peak level may represent the period of maximum hepatic necrosis, as the experimental work of Reissman *et al.* on dogs (*J. Lab. clin. Med.*, 1954, **43**, 572) has seemed to confirm. Of all the acute infectious diseases the only one known to cause marked elevation of the serum iron content is acute hepatitis. The authors therefore conclude that determination, and particularly serial determination, of the serum iron level early in the illness is definitely helpful in distinguishing between obstructive jaundice and acute hepatitis, and that it is of more value than the thymol turbidity test.

A. D. Duff

HAEMATOLOGY

829. The Mechanics of the "L.E." Cell Phenomenon Studied with a Simplified Test

I. SNAPPER and D. J. NATHAN. *Blood* [*Blood*] **10**, 718–729, July, 1955. 4 figs., 12 refs.

The authors, from the Beth-El Hospital, Brooklyn, New York, describe an L.E. test in which a drop of fresh blood from the patient is placed on an accumulation of dried polymorphonuclear leucocytes on a glass slide. After incubation the clotted blood is gently removed and the residual imprint of cells stained and examined. Thick leukaemic smears and imprints of carcinoma cells and of tissue from patients with Hodgkin's disease also provide suitable substrates.

The percentage of positive findings was equal to that by any other method and there have been no false positive results. The deoxyribose nucleic acid of the inclusion bodies obtained with this technique has undergone a greater degree of depolymerization than with other methods. If carcinoma-cell imprints are used the nucleoli persist in the inclusion bodies, suggesting that ribose nucleic acid does not undergo depolymerization with the L.E. factor. No L.E. cells appear to be deposited when a hanging drop of L.E. blood is placed on a clean slide. This is explained by the fact that, since the phagocytic leucocytes are still alive, the L.E. factor cannot reach their nuclei. However, depolymerization of the nuclei of dead leucocytes can occur, and these will be engulfed by polymorphonuclear cells that move out of the clot. The authors suggest that in the classic preparations it is the nuclei of non-viable leucocytes that are depolymerized, and these increase in number with the time of incubation. *E. G. Rees*

830. The Hematocrit of Capillary Blood

J. J. MCGOVERN, A. R. JONES, and A. G. STEINBERG. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 308–312, Aug. 25, 1955. 2 figs., 5 refs.

Wintrobe's well-known method for determination of the haematocrit value of venous blood has been universally accepted, but has the disadvantage that it is not readily applicable to infants and young children because of the difficulty of obtaining sufficient blood. The authors have therefore carried out, at the Children's Medical Center (Harvard Medical School), Boston, a revaluation of a micromethod proposed by Guest and Siler in 1934 (*J. Lab. clin. Med.*, **19**, 757) in which blood from a finger stab (the first drop being discarded) is collected into a 2–mm. capillary tube containing dried heparin; the tube is then sealed by heating and centrifuged for 5 minutes at 10,000 r.p.m. The exact technique is described in detail.

Haematocrit readings so obtained were tested for reproducibility and a coefficient of variation of 1 to 3% was obtained. Comparison of the results with those obtained by Wintrobe's method showed that the latter consistently gave a higher packed cell volume, but the difference was small and packed cell volumes ranging between 35 and 55% did not differ from those obtained by Wintrobe's method by more than 2 units. The correlation between the two methods was very high, the coefficient ranging from 0·933 to 0·957. The method described is recommended as being both simple and dependable. *Marjorie Le Vay*

831. The Amount of Trapped Plasma in the Red Cell Mass of the Hematocrit Tube

F. G. EBAUGH, P. LEVINE, and C. P. EMERSON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 409–415, Sept., 1955. 1 fig., 14 refs.

The concentration of erythrocytes as determined in venous or arterial blood is generally agreed to be some 8 to 10% higher than the "whole body haematocrit" reading. This discrepancy has been attributed by some workers to the presence of "trapped" plasma in the column of erythrocytes in the haematocrit tube or alternatively by others to an inequality in the distribution of erythrocytes between large and small blood vessels. In studies carried out at the Massachusetts Memorial Hospitals and Boston University School of Medicine, Boston, the authors have determined the amount of

plasma trapped in the cell column of the haematocrit tube in 52 samples of experimentally constituted anaemic, normal, and erythraemic blood. The cell volume was (1) measured directly by haematocrit readings and (2) indirectly computed from the dilution of radioactive chromium-labelled haemoglobin solution. The difference between these values was considered to represent the volume of plasma trapped in the packed cell mass of centrifuged samples of blood. The statistical methods employed are described and possible sources of error discussed. Data obtained in these studies indicated that a positive correlation exists between the quantity of plasma trapped and the height of the cell column. It was found that the amounts of plasma trapped were 0·8, 2, and 4% respectively for haematocrits of 40, 50, and 68%; these figures agreed well with those of Chaplin and Mollison (*Blood*, 1952, **7**, 1227) except that these authors reported significant amounts of plasma trapping at haemocrit readings below 30 volumes %, whereas the present authors could demonstrate no plasma trapping in blood samples with haematocrit readings of 33% or less. *A. W. H. Foxell*

832. Studies of Rh Sensitivity after Repeated Injections of Salk Vaccine

N. M. ABELSON, R. M. MCALLISTER, A. GREENE, and L. L. CORIELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 238–241, Sept. 24, 1955. 2 refs.

Because it was thought possible that poliomyelitis vaccine prepared on monkey kidney tissue might contain Rh antigenic material, samples of serum from 100 vaccinated children were tested at the University of Pennsylvania School of Medicine, Philadelphia. They were, however, found to be free from Rh antibodies. Two further investigations, using poliomyelitis vaccines, were made in which attempts to Rh-immunize volunteers were unsuccessful; the subjects in these studies comprised Rh-negative immunized as well as non-immunized individuals.

In a later study it was found possible to produce an immune response in some of the volunteers by injections of Rh-positive blood. It was also shown incidentally that all the lots of poliomyelitis vaccine used stimulated the production of poliomyelitis antibodies. The authors conclude that there is no likelihood of producing Rh immunization by the use of poliomyelitis vaccine of the Salk type. *John Murray*

833. V, a "New" Rh Antigen, Common in Negroes, Rare in White People

A. DENATALE, A. CAHAN, J. A. JACK, R. R. RACE, and R. SANGER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 247–250, Sept. 24, 1955. 1 fig., 5 refs.

In this joint paper from New York and London the authors report that a "new" antibody was recognized in the serum of a white male patient who, while under treatment at St. Luke's Hospital, New York, had received 26 blood transfusions, some of the donors being negro. This antibody detected an erythrocyte antigen occurring most frequently in West Africans, less frequently in New York negroes, and also, though rarely, in white subjects. In the subsequent investigation 168 New York negroes were tested for the new antigen and also for the A_1A_2BO, MNSs (including Hu, He, and Vw), P, Rh, Lutheran, Kell, Lewis, Duffy, and Kidd groups.

It was shown that the new antigen occurred more frequently in the presence of the Rh combination cDe or cde than would be expected by chance, whereas its presence appeared to be unrelated to that of any other type of blood group. Inheritance of the new antigen was demonstrated in negro and British white families to be a Mendelian dominant character. The gene for this new character appears to be part of some cde chromosomes and also of some cDe chromosomes, but its place in the Rh system is not clear. Because of the difficulties in defining the exact relationship of the new characteristic to the already known Rh antigens it is proposed to give it the temporary designation of "V". *John Murray*

834. Experimental and Statistical Studies on Rh Antibodies

V. I. KRIEGER and E. J. WILLIAMS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 199–224, Aug., 1955. 3 figs., 25 refs.

This long paper from the Royal Women's Hospital, Melbourne, is divided into four parts.

Part I discusses the various possible theories of action of blocking antibodies—that they act by preferential or competitive adsorption, or by neutralization of agglutinins—and the practical consequences to be expected in each case.

Part II describes the experimental work carried out to investigate the theoretical considerations discussed in Part I. These experiments showed that not all incomplete antibodies are blocking antibodies—indeed they revealed the existence of three types of incomplete anti-D antibody.

Part III discusses the authors' experimental findings and the published work of others, and presents evidence for the existence of five different physical types of Rhesus antibody—the saline type, three different types detected in serum albumin, and the cryptagglutinoid type detectable by the indirect anti-human-globulin test only.

Part IV incorporates the conclusions reached in Parts II and III in a suggested new interpretation of the results obtained by the various techniques for the estimation of Rh antibodies. According to this theory albumin titres measure the additive effect of incomplete and saline antibodies and, when the incomplete antibodies include no blocking antibodies, the difference between the saline and albumin titres represents the concentration of Type-2 incomplete antibodies. The original Wiener blocking test detects Type-1 incomplete antibodies, and Type-3 is the antibody which causes blocking in albumin. Type-5 is the cryptagglutinoid antibody and is the only one which is detected by the indirect Coombs test.

[This paper is written mainly for the serologist, and should be consulted in full by those interested in this field.] *I. Dunsford*

MORBID ANATOMY AND CYTOLOGY

835. Hyaline Membrane Disease of Newborn Premature Lungs. A New Approach
M. J. G. LYNCH and L. D. MELLOR. *Journal of Pediatrics* [*J. Pediat.*] **47**, 275–286, Sept., 1955. 9 figs., 18 refs.

Using the Lepehne–Pickworth and " Nadi " staining techniques, the authors examined frozen sections of both fresh and formalin-fixed material from the lungs of 4 newborn premature infants with typical hyaline-membrane disease at the General Hospital, Sudbury, Ontario, and compared the findings with those in similarly treated material from 11 control subjects, including adults, premature, stillborn, and full-term infants, and older children.

In the stained membranes many intensely blue granules were found, and similar granules occurred in the epithelium of the respiratory bronchioles and alveolar ducts with which the membrane was in contact. This finding, together with other evidence derived from histochemical studies, suggests that the membrane represents a concentration of the secretion of the respiratory bronchioles and alveolar ducts, and the authors comment on the frequent presence of excessive secretion in the bronchioles in premature infants. They postulate that the function of the substance which takes up the stain, which they believe to be an enzyme, is " to facilitate gaseous transfer in the lung " and that the amount secreted is proportionate to the concentration of oxygen in the inspired air. This hypothesis would explain the fact that membranes can be produced experimentally by exposing animals to high oxygen concentrations and that a reduction in the incidence of hyaline membrane has been reported to occur coincidentally with a reduction in that of retrolental fibroplasia on curtailing the use of oxygen in the treatment of premature infants.

[This paper would suggest that hyaline-membrane disease may be yet another iatrogenic disease to take its place alongside conditions such as pink disease and retrolental fibroplasia. However, as unsaturated fatty acids may equally well be responsible for the staining noted, and the distribution of the " enzyme " described corresponded closely to that of staining with the ordinary fat stains in hyaline-membrane disease, it is doubtful whether this new hypothesis will find general acceptance.]

Wilfrid Gaisford

836. The Pathology of Bronchial Asthma. I. The Significance of Membrane Changes in Asthmatic and Non-allergic Pulmonary Disease
S. B. CREPEA and J. W. HARMAN. *Journal of Allergy* [*J. Allergy*] **26**, 453–460, Sept., 1955. 5 figs., 11 refs.

In view of the widespread assumption that a thickened bronchiolar basement membrane is pathognomonic of bronchial asthma, lung tissue obtained from 116 necropsies performed at the University of Wisconsin Hospitals and from 107 lungs removed surgically for various reasons (mainly cancer, tuberculosis, and bronchiectasis) was examined histologically and compared with sections from the lungs of 22 patients with established bronchial asthma. As thickening of the basement membranes was frequently found in the lungs from non-allergic subjects it is therefore concluded that this cannot be regarded as a peculiarity of bronchial asthma alone.

H. Herxheimer

837. The Media of Small Muscular Pulmonary Arteries in Mitral Stenosis
R. M. O'NEAL, W. A. THOMAS, and P. M. HARTROFT. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **60**, 267–270, Sept., 1955. 4 figs., 9 refs.

Necropsy material from the lungs of 67 patients with mitral stenosis and 45 control subjects was examined at Washington University School of Medicine, St. Louis. No evidence of hypertrophy was found on measurement of the cross-sectional area of the media of small muscular pulmonary arteries. The selection of comparable arteries for measurement was based on the assumption that the branches of the pulmonary artery at the level of the respiratory bronchioles are constant in size. It was also assumed that the volume of the arterial muscle changes very slightly, and the length of the artery not at all, on contraction.

J. B. Enticknap

838. Pathological Findings in Nine Children with " Primary " Pulmonary Hypertension
M. BERTHRONG and T. H. COCHRAN. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **97**, 69–111, Aug., 1955. 48 figs., 38 refs.

The necropsy findings in 9 cases of pulmonary hypertension, 8 of which were in children under 5 years of age, are described. Pressure in the right heart had been measured during life in 4 cases, and ranged from 82 to 110 mm. Hg. In every case obstructive lesions were found in the pulmonary vessels, with no other demonstrable cause for the hypertension. The lesions found included arteriolar hypertrophy, intimal plaques, and intravascular thrombi. The authors believe that many of the vascular lesions were the result of organization of thrombi or intimal proliferation adjacent to such thrombi. Cyanosis was present in 6 cases and was associated with polycythaemia; in all these cases a small patent foramen ovale was found.

J. B. Enticknap

839. Changes in the Arterio-venous Anastomoses of the Heart Muscle in Hypertension. (Об изменениях артерио-венозных анастомозов сердца при гипертонической болезни)
A. V. ARKHANGEL'SKIĬ. *Архив Патологии* [*Arkh. Patol.*] **17**, 45–51, July–Sept., 1955. Bibliography.

The observations here reported from Saratov Medical Institute were based on histological studies of the heart of 20 persons whose death was directly due to hypertension, of 10 whose death was partly attributable to hypertension, and of 5 patients who died of chronic nephritis.

In the myocardium arterio-venous anastomoses arise predominantly from arteries of the short-circuiting type; these are most numerous in the wall of the left ventricle, but are also present in the walls of all four chambers as well as in the septa. Another type of anastomosis, in

which the vessel walls consist of so-called glomus cells, is best observed in the subepicardial fatty tissue at the base of the heart.

It appears that the anastomoses increase in number with age, and that in persons in the same age group they are much more numerous in those who are suffering from hypertension. On the other hand they were absent from the heart of a newborn baby, and also from that of a 19-year-old girl who died of chronic nephritis. Arterial changes due to hypertension are also followed by qualitative changes in the walls of the anastomoting arteries, consisting in hypertrophy and sclerosis with a consequent narrowing of the lumen. It was shown that the arterio-venous anastomoses in the hearts of persons who died of acute cardiac infarction, whether these patients were hypertensive or not, were fewer in numbers and "less pronounced". A detailed account of the histology of these anastomoses is given, and a bibliography of the Russian literature is appended.

A. Swan

840. **Basophilic (Mucinous) Degeneration of the Myocardium**

T. M. SCOTTI. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 994–1011, Sept., 1955. 12 figs., 21 refs.

The histochemical nature, morphological aspects, and incidence of "basophilic degeneration" of the myocardium, a condition which, according to the author, is often encountered but seldom described, are discussed in this paper from the University of Miami. Representative blocks from 7 regions from each of 75 hearts obtained at consecutive necropsies were fixed in 10% neutral formalin, and paraffin sections were stained with haematoxylin and eosin and by the periodic-acid–Schiff (P.A.S.) technique. The basophilic change, which affects the cytoplasm of scattered patches of myocardium, was seen in sections stained with haematoxylin and eosin taken from 53 hearts, the degree of change being considerable in one or more sections from 16. The commonest site was the left ventricle. Basophilic change was most frequently observed in hearts from subjects over 40 years of age; it was found, however, in hearts from 3 young subjects, aged 11, 13, and 16 years respectively. In affected fibres there was a strongly positive P.A.S. reaction, even after diastase digestion. These fibres were usually metachromatic with toluidine blue and stained light red with Mayer's mucicarmine. The mucinous material is regarded as a mucoprotein or acid mucopolysaccharide; it was commonly found in hearts containing abundant lipochrome pigment. No relationship was observed between the incidence of basophilic degeneration of the myocardium and sex, race, post-mortem autolysis, or concomitant disease process: in particular, there was no significant association with thyroid disease, anaemia, uraemia, or carditis.

The pathogenesis of the condition is not known, but the experimental work of Yokoyama *et al.* (*Arch. Path.* (*Chicago*), 1955, **59**, 347; *Abstracts of World Medicine*, 1955, **18**, 265) indicated an ischaemic basis.

A. Wynn Williams

841. **Intestinal Metaplasia of the Gastric Mucosa**

B. C. MORSON. *British Journal of Cancer* [*Brit. J. Cancer*] **9**, 365–376, Sept., 1955. 3 figs., 17 refs.

The author discusses the results of an investigation at Mount Vernon Hospital, Northwood, Middlesex, into the incidence and extent of intestinal metaplasia of the gastric mucosa. Strips taken from the entire length of the greater and lesser curvatures of stomachs removed at operations for duodenal ulcer, gastric ulcer, and carcinoma were examined histologically for the presence of intestinal metaplasia. Intestinal epithelium was observed in 93 out of 119 stomachs; it was most frequently found in cases of carcinoma and least commonly in cases of duodenal ulcer, cases of gastric ulcer being intermediate. In all three conditions the part of the stomach most frequently and extensively affected was the combination of pylorus and lesser curvature.

G. Calcutt

842. **Carcinoma Arising from Areas of Intestinal Metaplasia in the Gastric Mucosa**

B. C. MORSON. *British Journal of Cancer* [*Brit. J. Cancer*] **9**, 377–385, Sept., 1955. 13 figs., 17 refs.

At Mount Vernon Hospital, Northwood, Middlesex, histological examination of tissue from the primary growth and adjacent mucous membrane in 5 cases of carcinoma of the stomach showed that the tumour arose from epithelium of intestinal type. A detailed investigation of 107 cases of primary carcinoma of the stomach indicated that 30% of such growths arose from areas of intestinal metaplasia in the gastric mucosa. These findings are discussed in relation to the increased incidence of gastric carcinoma in patients with pernicious anaemia.

G. Calcutt

843. **Association of Gastrointestinal Carcinoid Tumor with Cardiovascular Abnormalities**

D. M. SPAIN. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 366–369, Sept., 1955. 6 refs.

The author has attempted to determine the incidence of the syndrome consisting in malignant carcinoid tumour of the intestine associated with hepatic metastases and some cardiovascular abnormality, most commonly fibrostenosis of the tricuspid and pulmonary valves. At the College of Physicians and Surgeons, Columbia University, New York, he found 26 cases of intestinal carcinoid tumour among a series of 8,000 consecutive necropsies, of which 500 selected at random served as a control group, the pathological findings in the two groups being then compared.

None of the latter showed any isolated fibrostenotic involvement of the pulmonary or tricuspid valves and less than 10% any evidence of developmental defects of the heart. In contrast, among the 26 cases of carcinoid tumour there were 9 (33%) with congenital cardiac lesions such as true Chiari's net, dextrocardia with atresia of the right auricle, or a pulmonary valve with 4 cusps, while in 10 cases there were non-rheumatic right-sided valvular lesions. In 24 of the 26 cases the primary tumour was in the intestinal tract; in 10 cases metastasis had occurred and 7 of these 10 patients showed

endocardial fibrosis with involvement of the tricuspid and pulmonary valves to a varying degree. Such cardiac lesions were present in only 3 out of the 16 cases without metastases.

The author discusses the possible aetiological relationship between carcinoid tumour and the cardiac lesions, with a brief survey of the literature. As carcinoid is often of developmental origin the cardiac lesion may be secondary to a metabolic abnormality associated with the tumour. Carcinoids originate from Kultschitzky cells; these cells are related to argentaffin cells which are known to secrete 5-hydroxytryptamine (serotonin), and large amounts of this substance have been demonstrated in carcinoid tumours. It has been suggested that the cardiac changes might be due to the deleterious effect of this substance on the endocardium, and that their predominance in the right side of the heart could result from the discharge of this material into the right heart from metastases in the liver. *F. Hillman*

844. **Florid Cirrhosis. A Review of 35 Cases**
H. POPPER, P. B. SZANTO, and M. PARTHASARATHY. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 889–901, Aug., 1955. 3 figs., 34 refs.

The hepatic condition described in this paper from Cook County Hospital, Chicago, and for which the name "florid cirrhosis" is proposed, is mostly seen in association with chronic alcoholism and has also been described under the names of chronic toxic hepatitis, progressive alcoholic cirrhosis, and subacute portal cirrhosis.

Necropsy material from 35 cases (selected out of a total of 11,743 post-mortem examinations carried out between 1946 and 1954) was studied. Most of the subjects were aged 27 to 50 years at death, 86% [30] were chronic alcoholics, and in 43% [15] there was a history of starvation and dietary imbalance. The average duration of illness was 76 days and the cause of death usually hepatic failure.

The liver was usually enlarged and its average weight was 2,240 g. Some macroscopic granularity was noted; the lobular pattern was generally obscured but not obliterated, though in some circumscribed areas it was exaggerated owing to centrilobular changes. Connective-tissue strands were barely discernible. In almost every case there were a few sharply defined lobules 2 to 3 mm. in diameter. The histological picture was extremely polymorphic, and varied even from area to area in the same liver. Parenchymal damage was always present. Nuclei were often pyknotic or absent. The cytoplasm was often clumped and contained refractile hyaline bodies. Granules of bile pigment were seen, but bile "lakes" and "casts" were absent. Regeneration was present in some areas, especially near necrotic parts, and the regenerated tissue did not have a lobular pattern. Centrilobular necrosis was present in 34% [12 cases] and collapse of some of the lobules in 46% [16].

Fatty metamorphosis was almost always present, especially in the centre of the lobule. Fine fibrous membranes were seen, especially in relation to the centre of the lobule and the portal tracts. Needle biopsy specimens in 15 cases showed the same type of lesion, but both fatty metamorphosis and necrosis were less in degree.

It is suggested that this condition, if untreated, progresses to Laennec's cirrhosis. The main aetiological factor in these cases appeared to be malnutrition, the condition being probably a stage in the fatty-liver-cirrhosis syndrome resulting from a deficiency of protein or lipotropic agents, or both. In addition, the damage to the hepatic cells resembled changes due to chronic toxic processes in a fatty liver and may have been linked with the secondary infection frequently present.

W. H. Horner Andrews

845. **Obstructive Biliary Cirrhosis and Alcoholic Cirrhosis. Comparison of Clinical and Pathologic Features**
C. A. DOEHLERT, A. H. BAGGENSTOSS, and J. C. CAIN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 902–914, Aug., 1955. 7 figs., 14 refs.

From the necropsy records of the Mayo Clinic for the period 1924-52 were selected 3 groups of 27 cases of cirrhosis of the liver of the following types: (1) early biliary cirrhosis, (2) advanced biliary cirrhosis, and (3) alcoholic cirrhosis, the purpose of the investigation being to compare the clinical and pathological features of the first two with those of the third. The biliary obstruction in each of Groups 1 and 2 was due to stones or strictures in 22 cases and to carcinoma in 5 cases. All the subjects had been jaundiced, the jaundice frequently being intermittent, and the average intervals between the onset of jaundice and death in the 3 groups were 2·9 years, 4·9 years, and 1·1 year respectively. Biliary cirrhosis was most frequently seen in association with intermittent jaundice of long duration, but could apparently occur when the jaundice was continuous. Ascites and gastric varices were commonest in Group 3, whereas bleeding other than from varices was more common in Groups 1 and 2. Some hepatomegaly was present in all groups, while splenomegaly was noted especially in Groups 2 and 3.

Degeneration and necrosis were seen in the liver in all groups. Fatty metamorphosis was found especially in Group 3, in which hyaline degeneration was also more frequent, a few cases only occurring in Group 2. Acidophilic degeneration was mostly seen in Groups 2 and 3, and atrophy in Groups 1 and 2. Necrosis was observed in all groups, both in the central and the peripheral parts of the lobule. Evidence of bile stasis was seen in almost all cases of biliary cirrhosis and in over 50% of those of alcoholic cirrhosis.

Leucocytic infiltrations were usually present, polymorphonuclear cells predominating in advanced biliary cirrhosis. Proliferation of the bile ducts was seen in all groups and particularly in Group 2. Large nuclei and dark cells were present in all groups, especially Groups 2 and 3, and in all groups the liver plates were two or more cells thick. Increased fibrous tissue was always present; in Group 1 it consisted of loose, irregular bands, in Group 2 it was similar, but more dense, while it was still more dense and more regular in its form in Group 3.

W. H. Horner Andrews

Microbiology and Parasitology

846. **Growth Factors for *Entamoeba histolytica***
M. NAKAMURA. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **89**, 680–682, Aug.–Sept., 1955. 7 refs.

Since *Entamoeba histolytica* was first cultured 30 years ago numerous attempts have been made to grow this organism in the absence of bacteria. The nearest approach to a pure culture was obtained by cultivation of the amoeba with *Trypanosoma cruzi*. In the present paper from the Boston University School of Medicine a new and successful method for propagation of *E. histolytica* free of bacteria is described. The amoebae were inoculated into Boeck–Drbohlav's diphasic medium, consisting of an egg slant covered with horse serum–Ringer's solution, to which were added rice powder, penicillin (15,000 units per ml.), and 0·5 ml. of the following sterilized mixture: 100 mg. per 50 ml. of adenosinetriphosphate, 100 mg. per 50 ml. of ribose-5-phosphate, diphosphopyridine nucleotide, and autoclaved bacterial cells (from the concomitant flora of the stock culture) grown on fluid thioglycollate medium. In the medium thus treated the bacteria associated with the amoebae were killed within 4 to 6 hours, leaving the amoebae to grow in pure culture for 9 days through 3 transfers, in the course of which their numbers gradually diminished until no further growth occurred in the fourth subculture.

It is concluded that this mixture, when added to the culture freed of bacteria, provided at least some of the growth-factors for *E. histolytica* which are usually supplied by the associated flora. However, failure to maintain subcultures indicated that some additional factors are required for the successful propagation of this organism.

C. A. Hoare

BACTERIA

847. **Antibiotic-resistant Staphylococcal Infection. A Study of Antibiotic Sensitivity in Relation to Bacteriophage types**
M. BARBER and J. BURSTON. *Lancet* [*Lancet*] **2**, 578–583, Sept. 17, 1955. 48 refs.

The senior author has for long been interested in the increasing incidence of penicillin-resistant staphylococcal infections in hospital, and in previous papers she and other workers have emphasized that such infections are, in most cases, due to cross-infection. Improved aseptic control appears to have failed to reduce cross-infection, and at the present time very significant numbers of strains of *Staphylococcus aureus* isolated from in-patients are resistant not only to penicillin but to streptomycin and the new tetracycline compounds.

In an attempt to determine the cause of this failure the present authors studied the nasal carrier rate of *Staph. aureus* in the maternity unit at St. Thomas's Hospital, London. In common with other observers they found that there was a very significant increase in the carrier rate among the mothers during their stay in hospital, and that *Staph. aureus* was present in nasal swabs from some 90% of the infants on discharge, the organism being penicillin-resistant in most instances. A significant proportion of the nursing staff were also carriers of penicillin-resistant strains. Employing the phage-typing technique the authors obtained evidence showing that the infants acquired the staphylococci from the nurses rather than from the mothers. Nevertheless, no serious infection developed in the infants.

The majority of these penicillin-resistant strains were sensitive to streptomycin and the tetracyclines. When, however, cultures of staphylococci isolated from true infective cases in other departments of the hospital were examined there was much more evidence of multiple resistance; half of the penicillin-resistant strains were also resistant to streptomycin and the tetracyclines. Most of the antibiotic resistance appeared to be associated with hospital cross-infection.

In an investigation of the relationship between antibiotic resistance and bacteriophage groups (Williams *et al. Lancet*, 1953, **1**, 510) it was found that the majority of the penicillin-resistant strains from the maternity unit belonged to Group I (Type 52A), whereas the resistant strains from true infective processes were mainly confined to Group III; indeed all strains exhibiting multiple resistance appeared to fall into Group III.

The authors suggest that successful control of the steadily growing antibiotic resistance of staphylococci depends on the prevention of hospital cross-infection and the intelligent use of all antibiotics.

H. J. Bensted

848. **The Interconversion of Diphtheroid Bacilli and *Corynebacterium diphtheriae* in Experimental Animals.** (Об изменчивости ложнодифтерийных палочек в организме экспериментальных животных)
B. L. PALANT, A. E. KHOLOD, and V. A. BLAGODETELEVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 30–35, No. 8, Aug., 1955.

The authors, working at the Metchnikov Institute for Vaccines and Sera, Kharkov, claim to have obtained the conversion of diphtheroid bacilli into *Corynebacterium diphtheriae* and vice versa by serial passages through white mice. Intraperitoneal injections of 1,000 million organisms of four different strains of *C. hofmanni* were given, and four typical strains of *C. diphtheriae* Type *gravis* were obtained in the 10th passage. The same result was obtained with one of the strains of *C. hofmanni* after the 5th intraperitoneal passage through normal guinea-pigs. Passaging of one strain of *C. diphtheriae* Type *mitis* and of the P.W.8 strain through white mice

in the same way resulted in their conversion to Type *gravis* after the first passage, whereas 3 other Type-*mitis* strains remained unaltered after the 13th passage. Passaging of 3 Type-*gravis* strains 5 to 10 times did not lead to any changes. However, passage of one Type-*gravis* strain through guinea-pigs immunized with alum-precipitated diphtheria toxoid converted it into *C. hofmanni*.

All the strains of *C. hofmanni* that had changed into *C. diphtheriae* Type *gravis* had become virulent in the process, and produced diphtheria toxin with an approximate M.L.D. of less than 0·05 ml. which could be neutralized by diphtheria antitoxin in the usual way. One Type-*gravis* and one Type-*mitis* strain of *C. diphtheriae* which had exhibited all properties of true *C. hofmanni* after passage through immunized guinea-pigs reverted to their original form on passage through white mice.

[As in many similar cases in which the stability of species and types has been disputed the authors did not use single-cell cultures in their experiments. Another objection to animal experiments of this nature is that the bacteria eventually cultured are not necessarily derived from the strain initially injected. The results here reported cannot, therefore, be regarded as conclusive evidence of the interconvertibility of diphtheroid and diphtheria bacilli.] *K. Zinnemann*

849. **Saccharose-fermenting Strains of *Corynebacterium diphtheriae*.** (О разлагающих сахарозу штаммах дифтерийного микроба)
V. M. Svetovidova. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 29–30, No. 9, Sept., 1955.

In the laboratories of the Department of Public Health, Tambov, Moscow, the author investigated the toxin-forming properties of 198 freshly isolated, saccharose-fermenting strains of *Corynebacterium diphtheriae*, having carefully excluded the possibility of contamination of the saccharose, the nutrient medium, and the strains themselves. Toxin was formed by 156 of these strains, while the remaining 42 were apathogenic. The majority of strains were found to dissociate on subculture into colonies of two different forms, in one of which the organisms had the usual rod-shaped microscopical appearance, while in the other they were more coccoid. Both forms, however, appeared to ferment saccharose, the coccoid form more rapidly than the other. Preparations of diphtheria toxin from two saccharose-fermenting strains, assayed by the intradermal method in guinea-pigs, were found to contain 66·6 and 90·9 minimum necrotic doses respectively per ml. The author concludes that, contrary to previous teaching, true pathogenic strains of *C. diphtheriae*, if freshly isolated, may be found to ferment saccharose, and this fact should not be overlooked when making a bacteriological diagnosis.

[This paper is of considerable interest to paediatricians and bacteriologists. It had been held that true toxin-forming strains of *C. diphtheriae* are unable to ferment saccharose until, in 1945, Frobisher *et al.* described certain strains which were capable of doing so. Any doubt about the purity of these strains was removed by Johnstone and McLeod, who obtained the same results from single-cell cultures. The author of the present paper obviously had no knowledge of this work, which makes her contribution all the more important as such strains have not hitherto been found by other workers.] *K. Zinnemann*

850. **Influence of the Method of Preparation and of the Structure of the Strain on the Quality of Toxic Substances Obtained from *Haemophilus pertussis*.** (Значение метода обработки и структуры штамма в характере токсических субстанций полученных из коклюшной палочки)
B. L. Palant, R. P. Fintiktova, and P. M. Mitelman. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 34–37, No. 9, Sept., 1955.

Although it is generally held that *Haemophilus pertussis* produces only an endotoxin, the authors have in the recent past (1949) obtained evidence of the production of an exotoxin by certain strains. In the work here reported from the Metchnikov Institute for Vaccines and Sera, Kharkov, antigen analyses were carried out on one strain (K2) which was capable, and on another (Kt) which was incapable, of producing exotoxin. When the two strains were subjected to tryptic digestion differences between the antigen complexes thus obtained could be detected by toxicity tests, and also by immunizing animals with these complexes and with antigens prepared by Boivon's method and challenging them with cultures, toxins, and isolated antigens. The lethal power of the toxic antigens on intraperitoneal injection into white mice and their necrotizing capacity on injection into the skin of guinea-pigs were estimated.

A loss of potency of K2 antigen prepared by tryptic digestion was recorded after heating for 60 minutes at 100° C., whereas antigen from the same strain prepared by Boivin's method and Kt antigens prepared by both methods were thermostable under the same conditions. The authors suggest that K2 antigen prepared by tryptic digestion contains both the thermolabile exotoxin and the thermostable endotoxin, whereas the other preparations contain only endotoxin. *K. Zinnemann*

851. **A New Method of Determining the Sensitivity of *M. Tuberculosis* to Chemotherapeutic Agents**
A. M. Beemer and C. H. L. Howells. *Journal of Clinical Pathology* [*J. clin. Path.*] 8, 242–244, Aug., 1955. 1 fig., 20 refs.

In this paper from the King George V Hospital, Durban, a simple plate technique for determining the sensitivity to streptomycin of *Mycobacterium tuberculosis* is described. The organism to be tested is streaked on the surface of Löwenstein–Jensen medium in a Petri dish, a culture of H37Rv being streaked on another part of the same plate. A strip of filter paper soaked in streptomycin–liquid-paraffin mixture is laid across the centre of the plate surface, and the whole is incubated for 10 days. After incubation confluent growth appears at a variable distance from this strip and the zones of inhibition are compared. It is claimed that the results

are in good agreement with those obtained by the serial dilution technique of Vollum. The method is recommended because results are obtained relatively quickly and examination of the cultures requires a minimum of technical skill. *E. G. Rees*

VIRUSES

852. **Studies in the Increase of Vaccine Virus in Cultured Human Cells by Means of the Fluorescent Antibody Technique**

W. F. NOYES and B. K. WATSON. *Journal of Experimental Medicine* [*J. exp. Med.*] **102**, 237–242, Sept. 1, 1955. 18 figs., 16 refs.

At the Sloan-Kettering Institute for Cancer Research, New York, the development of antigens of vaccine virus was observed in cultured human cells by means of the fluorescent antibody technique. The material used consisted of cultures of human epidermoid carcinoma cells (primary in larynx) which, when infected with a dermotropic strain of vaccine virus, were destroyed in 48 hours. Early (9 hours) after infection antigen was seen in very small amounts in the cytoplasm close to the nuclear membrane; in 16 to 24 hours progressively increasing amounts of particulate antigen were present in the cytoplasm. The size of the particles of antigen varied considerably, some cells containing large granules and others fine particles. With increasing concentration the antigen assumed a homogeneous form, this being due to close packing of particles or to soluble antigen, or to both. In later stages of infection homogeneous collections of antigen were seen in the nuclei. Cells which contained large amounts of antigen had cytoplasmic projections, which suggested that from these, by protoplasmic connexion, virus could be transmitted to uninfected cells; release of virus from these projections or from disrupted cells was another possible mode of spread of the virus. *Joyce Wright*

853. **Propagation of Influenza Virus in "Immune" Environments**

T. P. MAGILL. *Journal of Experimental Medicine* [*J. exp. Med.*] **102**, 279–289, Sept. 1, 1955. 11 refs.

An investigation into the propagation of influenza virus in an "immune" environment is reported from the State University of New York College of Medicine, Brooklyn. Influenza virus of the A/Berkeley–1/53 strain was passaged by intranasal inoculation in mice vaccinated with formalinized homologous virus suspension. Seven test antisera, each prepared with a different 1950-1 or 1952-3 strain, were used in haemagglutination-inhibition tests for investigation of the passage virus strains. Between the 2nd and 5th passages a variant occurred, the haemagglutination of which was more readily inhibited by the test antisera (including those prepared against 1951 strains) than was that of the parent strain. A 1951 strain (A/England–1/51) was then included in the vaccination procedure, and, later, a 1954 strain (A/England–1/54). The second variant, occurring between the 11th and 14th passages, was characterized by haemagglutination which was not inhibited by one antiserum (Kentucky–301/53v), but was still strongly inhibited by the remaining 6 antisera (2 prepared against 1950-1 and 4 against 1952-3 strains). The variants were affected more readily than the parent strain by antisera specific for the strains used in evoking the "immune" environment. Propagation of virus was accomplished with difficulty whenever the environment was altered, but once the series was established passage was readily continued. Variants were characterized by an altered antigenicity, and evoked antibodies in high titre specific for the variants and for three 1954 strains, although little or no inhibition was evident against haemagglutination by the 1950-1 strains. The findings were considered compatible with the concept that influenza virus has "a surface arrangement quite distinct from the inner virus bulk".

The pattern of influenza virus variation under experimental and natural conditions and the mechanism of virus variation are discussed. *Joyce Wright*

854. **Propagation and Primary Isolation of Mumps Virus in Tissue Culture**

G. HENLE and F. DEINHARDT. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **89**, 556–560, Aug.–Sept., 1955. 6 refs.

The authors have previously shown that egg-adapted mumps virus was capable of producing a cytopathogenic effect when inoculated into tissue cultures of monkey kidney epithelium or of human carcinoma (Strain HeLa) cells. These highly egg-adapted strains produced this effect, however, only when inoculated in large quantities, and failed to propagate in the tissue cultures. In the present studies, carried out at the Children's Hospital, Philadelphia, the authors show that strains which have undergone only a few passages in the chick embryo can be readily adapted to these tissue cultures and will produce a cytopathogenic effect when high dilutions of virus are inoculated. In HeLa cell cultures the effect was detectable 48 hours after inoculation and reached its maximum at 8 days; in monkey kidney cells it developed slightly more slowly. In ordinary tissue-culture tubes no production of haemagglutinin was observed, but infectivity end-points greater than 10^{-2} were not attained. In tissue-culture bottles in which infectivity titres of 10^{-4} were produced, haemagglutination titres of 1 in 16 were found.

The effectiveness of HeLa cell tissue cultures for primary isolation was compared with that of standard chick-embryo technique. Of 29 specimens of saliva from patients with parotitis, 20 gave a positive result by the former method, whereas only 14 out of 27 yielded virus by the latter technique; however, in 2 specimens from which no virus was isolated in tissue culture mumps virus was isolated in the chick embryo. A further advantage of tissue culture for isolation lay in the rapidity with which the presence of virus could be detected. Whereas typical cytopathogenic lesions in tissue cultures often developed within 3 days of inoculation, several passages of 5 or 6 days' duration were required before the virus could be detected by the pro-

duction of haemagglutinin in the amniotic fluid. With monkey kidney cell cultures the results were similar to those with HeLa cell cultures, although the presence of latent viruses in the former rendered them less suitable for primary isolation. *J. E. M. Whitehead*

855. **Fluorescent Antibody and Complement-fixation Tests of Agents Isolated in Tissue Culture from Measles Patients**
S. M. COHEN, I. GORDON, F. RAPP, J. C. MACAULAY, and S. M. BUCKLEY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **90**, 118–122, Oct., 1955. 3 figs., 10 refs.

SEROLOGY AND IMMUNOLOGY

856. **The Comparative Value of Whooping-Cough Vaccines. I. The Protecting Power of Sera Obtained by Immunizing Animals with Different Vaccines.** (К сравнительной оценке коклюшных вакцин. I. О защитном действии сывороток, полученных при иммунизации животных различными вакцинами)
N. N. SKLYAROVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 47–53, No. 9, Sept., 1955.

The investigation here reported from the Pasteur Institute, Leningrad, was designed to test the immunogenicity of both the thermostable and the thermolabile antigen components of *Haemophilus pertussis*. Three groups of rabbits were immunized: (1) with a boiled suspension of *H. pertussis*, (2) with a formolized suspension, and (3) with a suspension of living organisms, all being prepared from the same strain. The resulting agglutinating titres in the serum were 1 in 850 for Group 1 and 1 in 2,500 for Groups 2 and 3. The protective powers of serum from each group were tested in mice by giving up to 0·05 ml. intranasally 24 hours before infection by the same route with large doses (12·5 to 100 million organisms) or small doses (10,000 to 500,000 organisms) of *H. pertussis*. The quantity of serum required to protect 50% of the animals infected with the larger doses was 0·0035 ml. for Group-1, 0·0022 ml. for Group-2, and 0·0016 ml. for Group-3 serum. No such differences could be detected when the mice were infected with the smaller doses. The protective power of serum prepared with living vaccine was markedly diminished, but not completely lost, after removal of the antibody against the thermostable antigen by absorption with heat-killed bacterial antigen.

The author concludes: (1) that the thermostable component is an indispensable constituent of any vaccine against pertussis; (2) that the thermolabile antigen is equally indispensable for the production of highly effective vaccines; and (3) that formolization of such vaccines partly destroys the immunogenicity of the thermolabile antigen component. No conclusions are reached regarding the usefulness of this method of assessment for the clinical evaluation of the effectiveness of antipertussis vaccination. *K. Zinnemann*

857. **An Immobilization Test for Amoebiasis**
J. A. H. BROWN and J. L. WHITBY. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 245–246, Aug., 1955. 6 refs.

From the Royal Army Medical College, Millbank, London, the authors report the results of applying an immobilization test in parallel with the complement-fixation test for the diagnosis of amoebiasis.

For the complement-fixation test the antigens consisted of alcoholic extracts of washed concentrated suspensions of 3-day-old cultures of *Entamoeba histolytica*. Hyperimmune serum was prepared by giving rabbits a series of 10 intravenous injections of a concentrate of well-washed cultures of amoebae mixed with penicillin, 100 units per ml., and streptomycin, 100 μg. per ml. Preliminary tests had shown that with 2·5 M.H.D. of complement, fixation for 1½ hour at 37° C. was superior to other periods and temperatures. The antigens were used at concentrations of 1 in 8 and 1 in 16 and the antisera were tested at 1 in 4 and 1 in 8.

For the immobilization test, which was described by Cole and Kent (*Proc. Soc. exp. Biol. (N.Y.)*, 1953, **83**, 811; *Abstracts of World Medicine*, 1954, **15**, 287), amoebae were cultivated on Dobell and Laidlaw's medium, the authors being unsuccessful in obtaining adequate growth on a medium free from rice-starch, and a concentrate containing between 2×10^5 and 4×10^5 amoebae per ml. was used. Equal volumes of the serum under test and amoebic suspension were mixed in a tube, and a drop sealed under a coverslip and examined on a warmed stage at 37° C. The proportion of "rounded-up" immobile amoebae in a count of 25 was noted, immobile amoebae which were not "rounded up" not being regarded as immobilized. A reaction in which more than 70% immobilization occurred was regarded as positive, between 70% and 30% as doubtful, and less than 30% as negative. Immobilization is at a maximum after 30 minutes, after which the motility of many of the amoebae is restored. Sera which have not been inactivated by heat to destroy complement may cause lysis as well as immobilization.

Of 23 sera from active proved cases of amoebiasis and 2 from old cases with unproved but suspected recurrences, 6 gave positive, 3 doubtful, and 16 negative results in the immobilization test. The complement-fixation reaction was positive with 3 of the 25 sera tested, one of which gave a negative immobilization reaction. Although these results suggest that the immobilization test is superior to the complement-fixation test for diagnostic purposes, the authors consider the former to be less satisfactory than the latter because of its greater technical difficulty. They point out that as amoebic dysentery does not result in a high level of antibody in the blood it is hardly surprising that the interpretation of the complement-fixation test has never been satisfactory in this type of case.

[It is in the diagnosis of extra-intestinal forms of amoebiasis that serological tests can be of most value. It is generally recognized that some strains of *E. histolytica* are not satisfactory antigens, and that a good antigenic strain in the presence of rice-starch may become anticomplementary.] *C. L. Pasricha*

Pharmacology

858. **Influence of Chlorpromazine and Alcohol on Cerebral Hemodynamics and Metabolism**
J. F. FAZEKAS, S. N. ALBERT, and R. W. ALMAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 128–132, Aug., 1955. 10 refs.

In view of the possible use of chlorpromazine as a tranquillizing and anti-emetic drug in the treatment of acute alcoholic or immediate post-alcoholic states, the authors have investigated, in 21 convalescent patients at the District of Columbia General Hospital, Washington, D.C., the effect on the cerebral circulation of alcohol, chlorpromazine, and a combination of these drugs. In addition to determination of the cerebral blood flow, cerebral vascular resistance, and cerebral oxygen consumption, the mean arterial pressure was measured by means of a needle in the femoral artery. To 8 subjects 500 ml. of 10% ethyl alcohol was given intravenously over a period of 30 minutes; chlorpromazine was given intravenously to 7 subjects, of whom one received 300 mg. and the others 200 mg., while the remaining 6 subjects were given alcohol and chlorpromazine, or alcohol followed by chlorpromazine.

There was no significant increase in the oxygen consumption or cerebral blood flow with either drug. However the tranquillizing effect of chlorpromazine is produced, it does not seem to be associated with a reduction in the oxygen requirements of the brain. It was found that on those subjects who became hypomanic under the influence of alcohol the chlorpromazine had a good calming effect. The two drugs given together did not appear to have a synergistic effect and seemed to be acting on different parts of the brain. It is concluded that it is safe and beneficial to use chlorpromazine to quieten noisy alcoholics. *G. S. Crockett*

859. **Jaundice in Relation to Chlorpromazine Therapy**
B. ISAACS, J. G. MACARTHUR, and R. M. TAYLOR. *British Medical Journal* [*Brit. med. J.*] **2**, 1122–1124, Nov. 5, 1955. 15 refs.

860. **Clinical Investigation of a New Analgesic—Isopromedol.** (Клиническое исследование нового обезболивающего препарата изопромедола)
L. A. ZHEREBTSOV. *Советская Медицина* [*Sovetsk. Med.*] 29–33, No. 8, Aug., 1955.

"Isopromedol", an isomer of "promedol", is a colourless, crystalline substance soluble in water, alcohol, and acetone, but not in ether. Aqueous solutions can be sterilized by the usual methods. It has been shown to be 2 to 2½ times as effective in its spasmolytic effect as promedol, but less effective than "pantopon", which also has a more lasting action. Isopromedol has few side-effects, 2 patients out of 56 complaining of nausea and vomiting, and 2 others of headache, giddiness, and tinnitus. In one of these last (a case of radiculitis) convulsive spasm of the neck muscles occurred, lasting for about 12 minutes. The drug is an effective antispasmodic and is specially indicated for pain due to spasm of plain muscle (such as biliary colic), giving relief for 5 to 9 hours.

[This substance is allied to pethidine, its chemical designation being 1:2:5-trimethyl-4-phenyl-4-propionoxypiperidine hydrochloride.] *L. Firman-Edwards*

861. **The Effects of Glycyrrhetinic Acid on Salt and Water Metabolism**
E. E. GALAL. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **10**, 305–313, Sept., 1955. 4 figs., 19 refs.

Several reports have appeared of the deoxycortone-acetate-like activity in man of glycyrrhetinic acid (the active principle of liquorice), and some cases of Addison's disease have been successfully treated with this non-steroid substance. In this paper from the University of Edinburgh is described a full investigation of the relationship between deoxycortone acetate (DCA) and glycyrrhetinic acid in their effect on water and electrolyte metabolism in laboratory animals.

Urinary sodium excretion was studied in young female rats whose adrenal glands had been removed. The animals were divided into similar groups, some of which received glycyrrhetinic acid and some DCA, both substances being administered in propylene glycol by the intravenous or subcutaneous route or by stomach tube. The urine of each animal was collected over a period of 4 to 6 hours and its sodium and potassium content determined by flame photometry. The sodium excretion was not significantly inhibited in the rats treated with glycyrrhetinic acid provided that the urine was collected over a period long enough to allow adequate flow. Moreover, the drug did not maintain the blood sodium level and body weight, nor did it prolong the survival time of the rats, as occurred with DCA.

Glycyrrhetinic acid did, however, have a marked antidiuretic activity, independent of the method of administration, in both conscious and anaesthetized rats, although the degree of activity varied considerably from one animal to another. Water retention was also observed in a normal dog treated with the drug, and a similar effect was obtained in rats in which diabetes insipidus was brought about by removal of the posterior lobe of the pituitary gland. There was a significant delay in the absorption of water from the alimentary tract when the drug was administered by mouth, but not when it was given parenterally, so that inhibition of water absorption does not entirely account for the antidiuretic effect.

The author concludes that the action of glycyrrhetinic acid is different from that of DCA, and suggests that the reported favourable effects in Addison's disease may be due to the fact that in man the drug is metabolized in a different way. *Nancy Gough*

Chemotherapy

862. **Antifungal Activities of Bis*iso*quinolinium and Bisquinolinium Salts**

H. O. J. COLLIER, M. D. POTTER, and E. P. TAYLOR. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **10**, 343–348, Sept., 1955. 1 fig., 6 refs.

Polymethylene bis*iso*quinolinium compounds with 15, 17, and 19 methylene groups and a series of bisquinolinium salts with 11–14, 16, 18, and 20 methylene groups have been prepared. Polymethylene bis*iso*quinolinium salts with 10–20 methylene groups and the corresponding quinolinium salts were examined for activity against *Trichophyton mentagrophytes*. In both series, activity ncreased with increase in chain-length up to the tetradecamethylene member: a marked decline in activity was seen at the eicosane compounds.

The tetradeca- and hexadecamethylene members of both series were found to inhibit 11 strains of 6 species of pathogenic fungi in Sabouraud's broth at concentrations between 0.3 and 10 μg. per ml. The tetradeca- and hexadecamethylene bis*iso*quinolinium salts were slightly antagonized by hair and serum and the latter compound was potently antagonized by bovine bile. Exposure for 24 hours at 20° C. to hexadecamethylene bis(*iso*quinolinium methosulphate) did not destroy spores of *T. mentagrophytes* suspended in saline. On the other hand, viable spores could not be detected after incubation for 7 days at 27° C. with a concentration of 1.25 μg. per ml. of this compound in Sabouraud's broth.

The acute subcutaneous toxicities of the four tetradeca- and hexadecamethylene compounds and the acute oral toxicities of the two *iso*quinolinium compounds were determined in mice. Observations were also made on the acute intradermal toxicities and on the subacute toxicities to eyes and skin of rabbits. The results appeared to warrant clinical trial of the tetradeca- and hexadecamethylene bis*iso*quinolinium compounds in fungal infections of the skin.—[Authors' summary.]

863. **Effect of Penicillin on Group A Streptococci *in vivo* in the Absence of Leucocytes**

J. E. DARNELL, B. B. PESCH, and R. J. GLASER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 1237–1241, Aug., 1955. 5 figs., 27 refs.

In experiments carried out at Washington University, St. Louis, Missouri, the authors studied the effect of penicillin on Group-A streptococci *in vivo* in the absence of leucocytes. Using the method of Werner *et al.* (*J. clin. Invest.*, 1954, **33**, 742) they introduced 4-hour cultures of Group-A streptococci (S 23 Burbank) into the centre of agar disks (22 mm. in diameter and 15 to 20 mm. in height), which were then implanted into the peritoneal cavity of a rabbit. The bacteria immediately entered the logarithmic growth phase and multiplied at maximum rates for 8 hours; the growth curve showed a plateau after 18 hours, which persisted for 5 days. A fibrin–leucocyte membrane formed around the disks in approximately 24 hours, but leucocytes were unable to penetrate the agar. Large doses (30,000 units) of aqueous procaine benzylpenicillin injected intramuscularly into the rabbit either before or within 5 hours of implantation killed the bacteria in the disks within 4 hours, but doses injected 12 or more hours after implantation failed to do so. With repeated injections of procaine benzylpenicillin there was a decrease in the bacterial count, but some viable organisms remained.

The significance of these findings in the clinical treatment of streptococcal infection in man is discussed.

J. E. Page

864. **Clinical Studies of Carzinophilin, an Antitumor Substance**

N. SHIMADA, M. UEKUSA, T. DENDA, Y. ISHII, T. IIZUKA, Y. SATO, T. HATORI, M. FUKUI, and M. SUDO. *Journal of Antibiotics* [*J. Antibiot.*] **8**, 67–76, June, 1955 [received Oct., 1955]. 26 figs., 1 ref.

Carzinophilin, a substance isolated from *Streptomyces sahachiroi*, has been shown experimentally to inhibit the growth rate of several transplantable animal tumours, and to prolong the lives of the hosts. Its clinical application in 36 cases of malignant neoplasm in human patients is here reported from Keio University Medical School, Tokyo. The carzinophilin, which was injected intravenously since subcutaneous or intramuscular administration frequently resulted in induration, necrosis, and ulcer, was dissolved in 5% glucose solution to give a strength of 1,000 units of the drug per ml. Daily doses of 2,000 to 10,000 units, with totals varying from 50,000 to 820,000 units, were given, the total dose being determined by the appearance of side-effects; these took the form of nausea, loss of appetite, urinary excretion of urobilin, or leucopenia, the last-named occurring in nearly half the patients. So far 23 cases of malignant tumour have been treated which were considered to be inoperable, and 13 cases after radical operation in order to test the possibility of preventing recurrence. (The results in this latter group are not reported since the follow-up period is still too short.)

The 23 cases of inoperable tumour consisted of 10 of carcinoma of the stomach, 6 of carcinoma at other sites, 3 of reticulosarcoma, and one each of fibrosarcoma, Hodgkin's disease, teratoblastoma, and sarcoma. The resulting objective findings and subjective symptoms are presented in a table. In 4 cases ascites decreased, in 3 the tumour became smaller, and improvement in appetite or lessened pain was noted in 3; altogether the treatment had some beneficial effect in 8 out of the 23 cases. Six case histories illustrating the clinical course after treatment are described in detail. The authors conclude that favourable results may be expected in cases of sarcoma, Hodgkin's disease, and cancer of the skin.

H. G. Crabtree

865. **Study on the Treatment of Malignant Tumors in Childhood with Sarkomycin**

R. FUJII, J. ONIZAWA, N. SHIMA, K. OKUYAMA, and Y. OKAMOTO. *Journal of Antibiotics* [*J. Antibiot.*] **8**, 83–88, June, 1955 [received Oct., 1955]. 5 refs.

The anti-tumour action of the antibiotic sarkomycin and its low toxicity have been demonstrated in experiments with the Ehrlich carcinoma of mice, and in many clinical studies. This report from the University of Tokyo School of Medicine deals with the administration of sarkomycin to 12 children with malignant tumours of varying types, including 2 cases of cerebral tumour, 4 of leukaemia, and one of Hodgkin's disease. The initial dosage was 100 mg. daily, but this was soon increased to an average of 1 g., and occasionally to 4 g., daily. On account of the severe local irritation arising when other routes of administration were used the antibiotic was given intravenously in glucose solution.

The detailed clinical data which are given for each of the patients show that slight or transient improvement of subjective and/or objective symptoms occurred in 7 cases out of 11.

Untoward side-effects rarely occurred, and sarkomycin is recommended as an adjuvant to surgical operation and *x*-ray therapy. *H. G. Crabtree*

866. **Preliminary Results of the Use of a Colchicine Derivative, N-Deacetylthiocolchicine, in the Chemotherapy of Cancer.** (Premiers résultats de l'utilisation en chimiothérapie anticancéreuse d'un dérivé de la colchicine: la n-désacétyl-thiocolchicine)

R. HUGUENIN, R. TRUHAUT, and R. SARACINO. *Bulletin de l'Association française pour l'étude du cancer* [*Bull. Ass. franç. Cancer*] **42**, 308–325, 1955. 8 figs., 17 refs.

The mitostatic effect of the alkaloid colchicine has been known for a long time, but the severe toxic effects of even relatively small doses have precluded serious attempts to turn the antimitotic effect to therapeutic use. A number of less toxic derivatives of colchicine have been introduced from time to time which still retain the peculiar effect on mitosis, and the authors here record the results of their trials of three such derivatives at the Institut Gustave-Roussy, Paris—demecolcine, colchicoside, and N-deacetylthiocolchicine, recently synthesized by Velluz and Muller. This last substance appears to be about 7 times less toxic to animals, for the same mitostatic effect, than colchicine. Clinically, the results obtained by the use of the new compound in a small number of cases of myeloid leukaemia were not dissimilar from the familiar results of radiotherapy. However, an important observation was that satisfactory remissions could be induced by the new compound in patients who had become radioresistant. Not only was the leucocyte count reduced, but the spleen also was reduced in size and the general condition improved.

Perhaps the authors' most important observations were in the treatment of malignant growths. Although the administration of N-deacetylthiocolchicine alone had little effect, when used in association with radiotherapy some quite striking results were obtained. Thus in one patient with an extensive carcinoma of the floor of the mouth, recurrent after *x*-ray and radium therapy and surgery, complete resolution of the growth was obtained by the association of the new compound with deep *x*-ray therapy (3,000 r). A second case of carcinoma involving the floor of the mouth and submental lymph nodes responded equally well to 2,500 r in association with the colchicine derivative. [These doses of *x* rays are relatively small.] A surprising observation was that the injection of the compound was followed by quite marked focal reactions in the tumour, and occasionally the pain was so severe that morphine was necessary to control it.

[If these results can be confirmed in a larger number of cases, the introduction of this new colchicine derivative may signify a real advance in the treatment of malignant disease.] *W. M. Levitt*

867. **Antituberculous Activity of Cyanacetic Acid Hydrazide**

M. BARNETT, S. R. M. BUSHBY, R. GOULDING, R. KNOX, and J. M. ROBSON. *British Medical Journal* [*Brit. med. J.*] **2**, 647–649, Sept. 10, 1955. 1 fig., 9 refs.

The authors of this paper from Guy's Hospital Medical School, London, examined the toxicity and the antituberculous activity *in vitro* and *in vivo* of cyanacetic acid hydrazide (C.A.H.: "reazide") especially against strains of *Mycobacterium tuberculosis* resistant to isoniazid. C.A.H. was found to have antituberculous activity *in vitro*, but it was some 50 times less active than isoniazid. Against experimental infections in mice C.A.H. and isoniazid had the same relative antituberculous potency as *in vitro*, but were of the same order of toxicity. Strains resistant to isoniazid were generally also resistant to C.A.H., and this cross-resistance and the specific activity of both drugs against the tubercle bacillus strongly suggested that they act in the same way. However, the relative activity of the two drugs was not the same against all strains of tubercle bacillus, one strain, for example, being fully sensitive to C.A.H. yet moderately resistant to isoniazid.

The authors conclude that "from these experiments two important points emerge. Firstly, if C.A.H. is used alone in the treatment of tuberculosis there will be a big risk of isoniazid-resistant strains developing; secondly, it will be unusual for a patient with isoniazid-resistant strains to benefit from treatment with C.A.H." It is suggested that C.A.H. should not be used alone in clinical practice, as it is unlikely in most cases to be more effective than isoniazid. Nor should the two drugs be used in combination, as their effect *in vitro* and in mice is not additive. Indeed, C.A.H. seems to interfere with the action of isoniazid, reducing the activity of the mixture to a level approximating to that of C.A.H. alone. *E. Forrai*

868. **Antituberculous Activity of Tetracycline and Related Compounds**

G. L. HOBBY and T. F. LENERT. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 367–372, Sept., 1955. 2 figs., 5 refs.

See also Microbiology and Parasitology, Abstract 851.

Infectious Diseases

869. **Serum Amylase and Lipase in Mumps**
W. R. WARREN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 161–168, Aug., 1955. 4 figs., 15 refs.

The behaviour of the serum amylase and lipase levels in mumps was studied in 44 patients with typical manifestations of the disease. On admission the amylase level was raised in 36 patients and the lipase level in 8 (out of 11) patients. High initial serum amylase levels were observed in patients in whom the disease was severe, with high temperature, parotitis, and nausea and vomiting. There was no correlation between the rate of return to normal of the amylase value and the severity of the disease, or the prognosis, but the author considers that these determinations are of value in the initial diagnosis in atypical cases. The source of the increase of serum amylase appeared to be the parotid and intestinal glands, while the source of the increase of serum lipase was the intestinal glands only.

Winston Turner

870. **Effect of Physical Methods on the Mechanism of Breathing in Poliomyelitis**
G. J. BECK, G. C. GRAHAM, and A. L. BARACH. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 549–566, Sept., 1955. 4 figs., 13 refs.

Several methods of improving pulmonary ventilation in patients with partial respiratory paralysis following poliomyelitis are described and discussed in this paper from the Presbyterian Hospital, New York, and the Meadowbrook Hospital, Nassau County, N.Y. In one group of 13 patients breathing air a weighted sandbag or a stiff belt (Gordon–Barach) was applied to the lower abdomen; in 11 of these there was a decrease in ventilation of 11%, compared with a decrease of 13% in unassisted patients breathing 100% oxygen. In all but 2 cases a decrease in respiratory rate and an increase in tidal air occurred, improvement in dyspnoea being accompanied by a reduction in accessory muscle movements. Manual compression of the lower thorax at the end of expiration resulted in an increase of 6 to 77% in pulmonary ventilation in 8 out of 11 cases and an increase of 27% in vital capacity in 6 out of 9 cases.

Another method, exsufflation with negative pressure, was tried in 16 patients in whom respiratory insufficiency following poliomyelitis was responsible for difficulty in eliminating secretions. Gradual inflation of the lungs was achieved with a motor blower unit, positive pressure rising to 40 mm. Hg in 2 to 2·5 seconds. This phase was followed by a fall in 0·02 second to 40 mm. Hg negative pressure, which was maintained for 1 to 2 seconds. The cycle was then repeated. Lower pressures (± 20 mm. Hg) were used at first to accustom the patient to the apparatus; a mouthpiece similar to that used for estimation of the basal metabolic rate or a facemask was employed, the patient's cooperation being essential. Factors interfering with the efficacy of this procedure were voluntary closure of the glottis, gastric overdistension, and apprehension. An artificial "cough", which expelled secretions satisfactorily, was produced in all except 3 patients, one of whom had severe cerebral anoxia and 2 failed to cooperate. This method resulted in elimination or reduction of dyspnoea, cyanosis, and chest pain, outpouring of secretion or removal of mucous plugs, and re-aeration of atelectatic lung. In 8 out of 13 of the patients the use of the tank-type respirator was quickly discontinued. In 2 a tracheotomy did not interfere with efficient "cough", provided the stoma was plugged; application of the positive-negative pressure through the tracheotomy itself was not so effective. It is claimed that bronchoscopy is seldom required, and that exsufflation with negative pressure contributes to the weaning of the patient from the tank respirator to the cuirass.

D. D. C. Howat

871. **Treatment of Viral Hepatitis with the Knott Technic of Blood Irradiation**
R. C. OLNEY. *American Journal of Surgery* [*Amer. J. Surg.*] **90**, 402–409, Sept., 1955. 14 refs.

The author attempts to show that irradiation of the blood can be relied upon to terminate an acute attack of viral hepatitis, prevent recurrences, and arrest liver damage. The technique consists in withdrawing 1·5 ml. of blood per lb. body weight (3·3 ml. per kg.) from the patient, exposing it to radiant energy between the wave lengths of 2,399 and 3,900 Ångström units, and returning it to the patient through the needle used for the initial venepuncture. Treatment lasts 20 minutes and an average of three such treatments are given at 2-day intervals. In a series of 43 patients with hepatitis the average period of illness after treatment was instituted was 19 days.

[It is unfortunate that the series was uncontrolled; the results are of little value for assessing the effect of such treatment of a disease which has such a varied and unpredictable course.] *D. Geraint James*

872. **Anthrax. A Report of One Hundred and Seventeen Cases**
H. GOLD. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 387–396, Sept., 1955. 6 figs., 12 refs.

Since 1933 the author has encountered 116 cases of cutaneous anthrax, most of which occurred in a mill in Chester, Pennsylvania, where goat hair was used in the manufacture of interlining for coats. A sharp increase in the incidence of the disease was observed in the years 1940 and 1941, when war conditions led to a relaxation of regulations. The cases occurred in groups in close succession, usually related to the passage through the

mill of a new batch of hair. From samples of air and dust taken from the spinning and carding departments, in which no fewer than 74 of the cases occurred, *Bacillus anthracis* was recovered. A driver of a truck containing bales of hair contracted anthrax of the neck, and a girl aged 12 years became infected by washing a mill-worker's shirt.

The incubation period ranged from 12 hours to 5 days. Although in a number of cases a typical lesion developed at the site of skin trauma, some workers escaped anthrax in spite of severe puncture wounds sustained while working with heavily contaminated carding machines. Anthrax of the face and neck occurred in 47 cases.

The first 21 patients in the series were given intravenous injections of anti-anthrax serum; one of the patients died and in the remainder severe sensitivity reactions occurred. From 1939 until the introduction of penicillin and the broad-spectrum antibiotics sulphonamide therapy was given, sulphathiazole being the drug of choice. The author states that treatment with antibiotics offers the best chance of cure, provided dosage is adequate, effective results being obtained not only with penicillin but with chloramphenicol, oxytetracycline, tetracycline, and erythromycin. There was also one case of pulmonary anthrax but the bacteriological report of anthrax was not received until after the patient's death. *A. Garland*

873. **Erythromycin in the Treatment of Diphtheria and Diphtheria Carrier State**
M. W. Beach, W. B. Gamble, C. H. Zemp, and M. Q. Jenkins. *Pediatrics* [*Pediatrics*] **16**, 335–344, Sept., 1955. 8 refs.

While diphtheria antitoxin effectively neutralizes the exotoxin produced by *Corynebacterium diphtheriae*, the potential value of antibiotics in the treatment of diphtheria lies in the possibility of rapid elimination of the infecting organism from the nose and throat in the acute stage and in the carrier state. In view of favourable reports by other investigators of the effectiveness of erythromycin against *C. diphtheriae in vitro* and *in vivo*, the authors used this drug, together with diphtheria antitoxin, in the treatment of 49 patients with diphtheria who were admitted to Roper Hospital (Medical College of South Carolina), Charleston, having had no previous treatment. A positive culture of *C. diphtheriae* was obtained from the throat of 43 patients, of whom, it is stated, 29 gave consistently negative cultures after 24 hours of treatment, 4 after 2 days, 3 after 3 days, 2 after 4 days, 2 after 6 days, and one patient after 8 days. [Two patients are not accounted for in these figures; moreover, there appear to be a number of discrepancies between the results given in the text and those given in a long and detailed table.] Positive cultures reappeared in 2 cases during a period of probably somewhat irregular treatment at home after discharge; when re-admitted to hospital clearance was obtained on the 12th and 15th days of treatment respectively. One patient died of diphtheritic myocarditis on the 13th day. Positive throat cultures were obtained from an additional series of 5 persons without clinical evidence of infection, who were consequently regarded as carriers. Cultures were consistently negative in 3 of these cases after 24 hours, in one after 3 days, and in one after 9 days of treatment with erythromycin.

The drug was given in the form of a suspension of erythromycin ethyl carbonate, the dosage ranging from 25 to 50 mg. per kg. body weight daily, given at 4- to 6-hourly intervals. The average duration of treatment was 10 days.

The authors consider that the results obtained with erythromycin in this series are superior to those obtained with other antibiotics tested by different investigators by comparable methods. *K. Zinnemann*

874. **A Comparison between the Results of Bacteriological Cultures of Blood and of Bone Marrow from Patients with Typhoid Fever Treated with Syntomycin.** (Сравнительная оценка бактериологического исследования крови и пунктата грудины у больных брюшным тифом, лечившихся синтомицином)
I. G. Bulkina, L. D. Balanchuk, and V. I. Pokrovskiĭ. *Терапевтический Архив* [*Ter. Arkh.*] **27**, 37–41, No. 6, 1955. 11 refs.

At the First Lenin Medical Institute, Moscow, samples of blood and bone marrow from 30 patients suffering from typhoid fever, bacteriologically confirmed and treated with "syntomycin", were cultured in approximately five times their volume of bile. It was found that on the 5th day of treatment bone-marrow culture gave positive results more often than blood culture. After 6 days of treatment both cultures gave negative results. In the early stages of the disease bone-marrow culture was found to be positive in 85·4% of cases, as against only 41·7% of cases by blood culture. No relation was observed between the degree of pyrexia and the proportion of positive results of bone-marrow culture. *A. Swan*

875. **The Clinical Course of Typhus Fever in Sporadic Cases.** (Современное клиническое течение сыпного тифа)
G. M. Kapnik. *Терапевтический Архив* [*Ter. Arkh.*] **27**, 42–50, No. 6, 1955. 4 figs., 13 refs.

The author reports that sporadic cases of typhus fever, as distinct from those seen in an epidemic, are characterized by a much milder degree of toxaemia and of involvement of the central nervous system, as well as by a relatively intact cardiovascular system. The temperature curve retains its cyclical form, but the period of pyrexia is reduced to 7 to 10 days and the peak of temperature rarely exceeds 40° C. (104° F.). Convalescence is more rapid and complete than in the epidemic form, while complications are rarer. Agglutination reactions, such as the Weil–Felix reaction, the rickettsial agglutination reaction, and the complement-fixation test, become positive in diagnostic titres late in the course, that is, on the 9th to 11th day of illness or about the beginning of convalescence. In the treatment of sporadic cases of typhus fever the use of the antibiotics "syntomycin", "laevomycin", and "biomycin" is recommended. *A. Swan*

Tuberculosis

876. **The Treatment of Primary Tuberculosis with Isoniazid.** (Die Isoniazid (INH)-Behandlung der primären Tuberkulose)
I. HOFFMANN and I. TELEGDI. *Zeitschrift für Tuberkulose* [*Z. Tuberk.*] **106**, 232–235, 1955.

Isoniazid was used in the treatment of 224 children with primary tuberculous infection at the State Sanatorium for Children, Szabadsághegy, Hungary. The dose employed was 5 to 10 mg. per kg. body weight daily. Most active cases became quiescent in four months. [The criteria of "activity" are not stated.] Radiological improvement was common, especially in those under 3 years of age. In 31 cases there was bronchoscopic evidence of rupture of caseous lymph nodes into the bronchus and in 9 of these further bronchoscopy was necessary 4 to 5 months later for the removal of caseous debris. In this respect isoniazid was of no apparent benefit. No toxic symptoms were observed from isoniazid during prolonged courses lasting for 3 to 12 months.

No child who received isoniazid developed meningitis or other complications during or after treatment. This last observation leads the authors to recommend that all children recently infected with tuberculosis should be given a course of isoniazid lasting 3 to 5 months.

[It is impossible to draw any conclusions from this paper. Primary tuberculosis in childhood is a naturally benign condition and only a strictly planned and fully controlled trial can prove the effectiveness of any line of treatment. This has not been attempted.]

John Lorber

DIAGNOSIS AND PROPHYLAXIS

877. **Tuberculous Morbidity among Warsaw Children Vaccinated with B.C.G.** (La morbidité tuberculeuse chez les enfants vaccinés au B.C.G. à Varsovie)
H. ZAPASNIK-KOBIERSKA and M. STOPNICKA. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **19**, 369–383, 1955. 5 figs., 11 refs.

The authors describe the results of an investigation of 205 children who had been vaccinated with B.C.G. and who were referred as possible cases of tuberculosis to the Central Antituberculous Dispensary, Warsaw.

After extensive investigation 22 patients were considered to present evidence of tuberculous infection, 15 having involvement of mediastinal nodes (in 4 cases associated with atelectasis), 2 having pleural effusion, one tuberculous uveitis, and 4 calcified mesenteric nodes. Of these children, 7 appeared to have been vaccinated during the pre-allergic phase; the others had remained in contact with open cases of tuberculosis, one having been heavily infected 1½ years after vaccination by a parent dying of the disease.

In the remaining 183 cases, many of which were referred to the Centre with radiological and clinical diagnoses of tuberculous infection of the mediastinal nodes or pulmonary infiltration, the diagnosis of tuberculosis was not confirmed; many of the children were suffering from sinus and adenoidal infection. In some of these cases the diagnosis of tuberculosis had been based on a positive Mantoux reaction or was due to failure to elicit a history of vaccination with B.C.G. The authors state that in general tuberculous infection after B.C.G. vaccination is rare and when such infection appears to be present other causes must first be sought. In a very few adequately vaccinated cases a mild superinfection may occur. *J. Robertson Sinton*

878. **The Effect of Repeated Tuberculin Testing on Post-vaccination Allergy. A Preliminary Note**
K. MAGNUS and L. B. EDWARDS. *Lancet* [*Lancet*] **2**, 643–644, Sept. 24, 1955. 1 ref.

The authors present from the World Health Organization Tuberculosis Research Office, Copenhagen, some preliminary observations on the area of induration of the intradermal tuberculin reaction after B.C.G.-vaccination and the persistence of post-vaccination sensitivity.

An early survey of the reaction to 10 units of P.P.D. was made in children who had been tested annually and compared with that in those tested for the first time either 3 or 4 years after vaccination. This gave results which suggested that the degree of allergy might be greater in the former group, and further evidence provided by a second and larger survey has appeared to confirm this. The second survey showed that in 114 subjects tested for the first time after 3 years the reaction averaged 12·0 mm. in diameter, while in 54 subjects who had been tested annually the mean diameter was 18·6 mm., a difference of 6·6 mm. The corresponding difference in another group after a 4-year interval was 8·2 mm. The authors recognize that these figures have been obtained in a trial which was neither extensive nor systematic and they suggest that a further controlled trial should now be undertaken. *John M. Talbot*

879. **Importance of Tuberculin Testing of School Children—a Twenty-eight Year Study.**
J. A. MYERS, F. G. GUNLAUGSON, E. A. MEYERDING, and J. ROBERTS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 185–190, Sept. 17, 1955. 2 figs., 17 refs.

Inspired by an estimate made by Krause in 1926 of the potential value of serial tuberculin testing in the epidemiology of tuberculosis, the authors initiated a long-term study in which tuberculin tests were performed on the children in 24 Minneapolis schools at intervals of approximately 10 years, original tuberculin being injected by the intracutaneous route on each occasion.

In 1926 and 1936 the usual procedure was adopted of giving those children not reacting to the first strength a second and larger dose, whereas in 1944 and 1954 a single dose of 1 mg. was given. An area of induration or oedema, or both, 5 mm. or more in diameter was regarded as a positive reaction.

In 1916 it had been estimated that 70% of Minneapolis children became infected during the first 14 years of life. In 1926 47.3% of the school-children tested reacted to tuberculin, showing that the risk of infection, although less, was still great. Efforts were then intensified in the city to segregate infectious persons and to discover cases among the general population. By 1936 the incidence of tuberculin-positive children had decreased to 18.9% and by 1944 to 7·7%. Improved facilities for treatment had become available during this period, and legislation providing for compulsory segregation of recalcitrant patients had been introduced. Between 1944 and 1954 the number of cases of tuberculosis decreased to such an extent that there was no significant waiting list for sanatorium beds. A mass radiography survey in 1947 reached approximately 64% of the adult population. Further, bovine tuberculosis throughout the State of Minnesota was reduced to vanishing point. In 1954 out of 11,818 children tested (98·7% of the school population in the same 24 schools) only 3·9% were positive reactors.

Attention is drawn to the case-finding value of this type of project and to the preventive value of the periodic examination of reactors. "The tuberculin test", it is asserted, "has become the master key to the tuberculosis problem", enabling tuberculosis to be detected in the individual at the earliest possible moment, and providing the means of measuring the size of the tuberculosis problem in the community and the effectiveness of preventive measures. If, as recently recommended by Waring, antimicrobial drugs are given as soon as possible after the reaction becomes positive, it may be possible to destroy all the infecting tubercle bacilli before they become inaccessible in necrotic lesions.

Norman F. Smith

880. **Tuberculosis in Students and Nurses**

R. E. VERNEY. *British Medical Journal* [*Brit. med. J.*] 2, 929–934, Oct. 15, 1955. 1 fig., 11 refs.

The incidence of tuberculosis in students of all faculties at the Universities of Edinburgh, Glasgow, Cambridge, and Belfast over the 3-year period 1950–3 and the results of B.C.G. vaccination of students and nurses at ten university centres are reported. At the four named universities over 43,000 students were examined; it is pointed out that to begin with examination was optional, but in the last two years of the period a degree of compulsion was introduced at Edinburgh which resulted in 84% of the student population being included in the survey. The investigation consisted in mass radiography, Mantoux tests (initially the Mantoux test with old tuberculin was used, but later Heaf's multiple-puncture method was adopted), B.C.G. vaccination of negative reactors, and careful follow-up of proved and doubtful cases.

The average incidence of pulmonary tuberculosis in all students of the four universities during the period under review varied from 1·5 per 1,000 (Cambridge) to 3·4 per 1,000 (Belfast). Tuberculin-sensitivity tests carried out on 11,065 first-year students and nurses at ten university centres revealed that the percentage of negative reactors at these centres varied from 20·9 to 36·4 (average 27·6). Altogether 2,630 of these tuberculin-negative subjects received B.C.G. vaccine with no untoward effects, but 0·11% failed to convert and 1·44% reverted to negative within 5 years. In this group the subsequent incidence of tuberculosis was only 0·1% compared with 3·3% in a control group of 392 non-vaccinated tuberculin-negative subjects.

The author discusses the "ominous" significance of extreme skin sensitivity to tuberculin and the pathogenesis of pulmonary tuberculosis in young adults. He points out the advantages which would accrue if all students were required to undergo physical examination before they could matriculate, and emphasizes the desirability of B.C.G. vaccination of all tuberculin-negative subjects.

[This is an excellent report and a valuable supplement to the Prophit Survey of 1948.] *R. J. Matthews*

EXTRA-RESPIRATORY TUBERCULOSIS

881. **The Treatment of Tuberculous Meningitis since the Introduction of Isoniazid.** (Unsere Erfahrungen seit der Einführung des Isoniacid (INH) in die Behandlung der Meningitis tbc)

I. FLESCH, G. PINTÁRÉR, G. SZÖKE, and É. TÓTH. *Zeitschrift für Tuberkulose* [*Z. Tuberk.*] **106**, 217–227, 1955. 2 figs., 32 refs.

Between April, 1952, and December, 1953, 77 children suffering from tuberculous meningitis were treated with isoniazid for at least 3 weeks at the State Children's Sanatorium, Budapest. [The number of those who received less than 3 weeks' treatment is not stated.] In 69 of these cases streptomycin was also given, by the intramuscular route only in 70%, for an average of 4 months. Isoniazid was given by mouth in small, medium, or large daily doses (2·5 to 5 mg. per kg. body weight, 5 to 8 mg. per kg., and 8 to 10 mg. per kg. respectively), 66% of the children receiving the small dose. The duration of isoniazid treatment varied between 2 and 9 months. There were no toxic symptoms.

Of the 69 patients who received the combined treatment, 10 were under 2 years of age, 8·5% were unconscious on admission, and 17% had associated miliary tuberculosis. All but 4 (94·2%) survived, and of the 65 survivors, 49 (75·4%) made a complete recovery. Some of the others were suffering from sequelae or still had abnormalities in the cerebrospinal fluid (C.S.F.), while others were still being treated at the time of the report. The period of observation was very short, only 8 patients having been followed up for 12 to 18 months after the conclusion of treatment. Of the 4 patients who died, 3 were admitted in coma and the fourth had extensive generalized tuberculosis.

In the authors' opinion the clinical course of the disease has become shorter since the introduction of isoniazid, and the most rapid improvement was noted when the dose of isoniazid was 5 mg. per kg. daily. The C.S.F. usually returned to normal within 4 months of apparent clinical recovery, while miliary shadows on radiographs of the chest disappeared between 1 and 4 months after recovery. In two-thirds of the cases the tubercles of the choroid disappeared after about 6 months. Repeated air encephalography showed that in 54% of cases the ventricles were of normal size throughout, and of those admitted with hydrocephalus, regression or return to normal occurred during treatment in 70%. Only 2 children developed a spinal block. One child developed optic atrophy and became blind.

Relapses and recrudescences were not uncommon 6 to 10 months after the beginning of treatment (18% and 20% respectively), but further treatment led to uneventful recovery. Relapses occurred most commonly in those patients who were treated for only 3 months with small doses of isoniazid.

[The very high survival rate without intrathecal treatment claimed here is unacceptable, as an unstated number of deaths which occurred during the first 3 weeks of treatment have been excluded from consideration. As the few deaths which occur with modern treatment usually fall within this period, their exclusion completely falsifies the results. Other conclusions drawn by the authors are also unwarranted: for example, the relatively small dose of 5 mg. per kg. is stated to give better results than larger doses. But it is not stated how the dosage to be given to each patient was determined; if the small dose was reserved for early cases and the large dose for late cases the former may have done better in spite of, rather than because of, the smaller dosage. The high relapse rate and the short follow-up period are other features which should be taken into consideration in evaluating the authors' conclusions concerning this method of treatment.]

John Lorber

882. **The Subsequent Fate of Children after Recovery from Tuberculous Meningitis.** (Zur Frage des weiteren Schicksals der Kinder nach geheilter Meningitis tbc)
E. POST. *Medizinische* [*Medizinische*] 1299–1304, No. 37, Sept. 10, 1955. 5 figs.

The results are reported from the Children's Hospital, Essen, of a neurological and psychological assessment of the condition of 40 children who had recovered from tuberculous meningitis more than 2 years previously, having been treated between 1948 and 1951. These 40 children consisted of 30 of the 35 survivors out of 120 treated in the hospital during that period, together with 10 others whom the author had an opportunity to study. It was concluded that the majority of these children could be rehabilitated within their families and that most of them would be able to earn their livelihood in due course.

The sequelae observed are classified as follows. (1) Those due to streptomycin: complete or partial loss of hearing in 11 cases; complete or partial loss of vestibular function in 24. (2) Those due to the meningoencephalitic process: a total of 30 instances of 12 different types of neurological abnormality were found, including 2 instances of hemiplegia and one of partial optic atrophy. (3) Primary diencephalic symptoms: a total of 65 instances of 9 different conditions were found, including 14 cases of polydipsia, one of diabetes insipidus, 2 of precocious puberty, 24 of vegetative disturbances (such as undue sweating, tremor, and sudden changes of colour), 6 of headaches, and 5 of sleep disturbance. (4) Postencephalopathic symptoms: a total of 58 instances of 9 types of disturbance were noted, including sensitivity to light and noise, irritability, emotional lability, and lack of initiative.

The intelligence of the group as a whole was only moderate, even when the effects of the long illness, and the absence from school of those of school age for about 2 years in most cases, were taken into consideration. Only 4 out of the 24 of school age could hold their own with schoolmates of the same age group, and only 14 were considered to be within the normal average range of intelligence. The degree of retardation was considerable in 5 children, while 2 children had suffered major psychological damage. Many of the sequelae, however, were alleviated by physical or psychological treatment.

[This paper does not give a clear picture of the group as a whole, as emphasis is placed on the lesions and not on the individual patient. The results of treatment were poor in terms of survival and apparently also in terms of the condition of the survivors as compared with those reported from many other major European and British centres.]

John Lorber

RESPIRATORY TUBERCULOSIS

883. **Tuberculous Pleurisy with Effusion**
J. A. MYERS. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 191–201 Aug., 1955. 12 refs.

In this paper from the University of Minnesota an analysis is presented of 260 cases of tuberculous pleural effusion in patients ranging in age from 1 to 80 years, 95 being between 20 and 24 and 65 between 25 and 29. There were 139 females and 121 males, and the effusion was on the right side in 141 cases. The most frequent first symptom was pain, which was followed by a rise of temperature. The physical signs of any early effusion are difficult to elicit, and *x*-ray examination is often necessary for its detection, while the ultimate diagnosis of the nature of the effusion must rest upon the demonstration of tubercle bacilli in the fluid. In 68 cases in this series aspiration was not carried out, and in 116 of those cases in which it was performed tubercle bacilli were not found or no report was available. In some of these cases the condition may have been non-tuberculous although all the patients reacted positively to tuberculin.

The observations reported were made over a period of 35 years, and changing opinions about the nature of this condition are reflected in the treatment employed. At first the fluid was not removed (68 cases); later,

artificial pneumothorax following removal of the fluid became popular; and later still, when it was learned that extensive deposits of fibrin from residual fluid limited the function of the lung, complete and repeated aspiration was advocated. Only in 94 cases did the condition clear up so completely that there was no abnormality on subsequent radiographs. The author now recommends that the effusion be aspirated and the pleural space kept as dry as possible, that strict bed rest be maintained for 6 months, or longer if necessary, and that chemotherapy be given as for pulmonary tuberculosis. Occasionally, if there is evidence of fibrin deposit when the patient is first seen, decortication should be considered.

Immediate prognosis is good, and remote prognosis depends upon the nature of the underlying cause rather than on the size of the pleural effusion. In 55 cases in the present series there was evidence suggestive of a primary pulmonary lesion, yet only in 3 did clinical pulmonary disease subsequently develop. Of the 260 patients, 13 could not be traced and 11 had died from non-tuberculous conditions at the time of follow-up. Of the remaining 236, 5 had been treated for pulmonary tuberculosis at the time of the effusion or within the next 3 years because of slight *x*-ray changes at the site of a primary focus, although none presented clinical symptoms of the disease. Tuberculosis of the reinfection type subsequently developed in 23 cases, the lesions being extrathoracic in 10. In only 3 of these 23 was primary infiltration of the lung detected radiologically at any time.

It is suggested that chemotherapy administered promptly after tuberculin conversion, when the lesions are small and vascular, may prevent sub-pleural lesions from involving the pleura and causing pleurisy with effusion as well as other forms of clinical tuberculosis.

Kenneth Marsh

884. **"Modified" Thoracoplasty**

T. Holmes Sellors, J. W. Jackson, and J. G. Callanan. *Thorax* [*Thorax*] **10**, 191–196, Sept., 1955. 5 figs., 5 refs.

The authors, writing from the London Chest Hospital and Harefield Hospital, Middlesex, describe a one-stage thoracoplasty designed to avoid deformity and post-operative paradoxical respiration as well as to prevent re-expansion of the mobilized apex and the "creeping" upwards of the lung so commonly seen in emphysematous patients with persistent cough. In this operation, which is carried out through the usual thoracoplasty incision, a rib-flap consisting of the 2nd, 3rd, 4th, and, sometimes, the 5th ribs, which have been divided front and back, is turned inwards over the mobilized apex and fixed in position by sutures. To fashion the flap the posterior ends of the ribs to be mobilized are excised as near the transverse process as possible, the corresponding intercostal bundles being divided. The periosteum is stripped from the under-surface of the 1st rib and the usual apicolysis is carried out as far as the hilum. The 2nd and 3rd costal cartilages, when exposed, are divided in turn, and the 4th rib is divided in the axillary line. The flap so formed is hinged on the 4th or 5th intercostal muscle and turned inwards and downwards so that the 2nd rib and 1st bundle lie at the lung root against the mediastinum. The posterior ends of the ribs are sutured to the periosteum at the 6th or 7th vertebra posteriorly, and the 2nd costal cartilage is sutured to the mediastinum at the level of the 3rd interspace. The space remaining between the 2nd rib and the mediastinum is closed by several fine sutures.

This operation has been performed on 135 patients, in 20 of whom the thoracoplasty was combined with resection. There were 2 postoperative deaths—one from cerebral thrombosis and one from pulmonary stenosis, the severity of which was not recognized. The most common complication was a blood-stained effusion, following a pleural tear, which, however, responded well to aspiration. In 5 cases there was ipsilateral post-operative atelectasis. Contralateral spread was not observed in any of the cases, while extension or re-activation of the disease, although suspected in 4, was observed radiologically in only 2 cases. A late complication was re-expansion of the apex, considered to be due to imperfect fixation of the flap to the mediastinum.

A follow-up investigation 6 months to 4 years after operation revealed cavity closure in all the 87 who originally had a patent cavity, and sputum conversion in 75 of the 78 with a positive sputum at the time of operation; in the 3 patients whose sputum was still positive there was obvious disease on the opposite side.

In general, the authors employed this technique in patients with fairly stable, localized disease. They consider that it is particularly valuable as a limited procedure in patients with bilateral disease, in young women (to minimize deformity), and in elderly patients with emphysema.

A. M. Macarthur

885. **Clinical and Bacteriological Study of Resected Tuberculous Pulmonary Lesions**

F. Amoruso. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] 73, 435–442, Sept. 15, 1955. 18 refs.

The clinical, bacteriological, and histological findings in 132 cases of pulmonary tuberculosis in which resection was performed are analysed in this paper from the Saskatoon Sanatorium, Saskatchewan. The cases were divided into 4 groups according to the type of lesion and extent of the disease as follows: (1) tuberculomatous lesions (14 cases); fibrocaseous lesions (14); cavitary lesions (56); and far-advanced disease with destruction of lobes or lungs (48). In all cases chemotherapy was given for 6 to 18 months before operation, which was performed at the stage of maximum clinical and radiological improvement. In spite of this tubercle bacilli were found on microscopy in 82·5% of the resected specimens, and in 27% the bacilli were cultured or were found to be pathogenic to guinea-pigs. The percentage distribution of the organisms, both stainable and viable, was practically the same regardless of the type of lesion and extent of the disease, provided there were areas of caseation.

At the time the paper was written almost all the patients had been discharged and were well.

E. G. Rees

Venereal Diseases

886. **Erythromycin and Tetracycline Hydrochloride in the Treatment of Non-gonococcal Urethritis**
R. R. WILLCOX. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 186–187, Sept., 1955. 1 ref.

The results obtained at St. Mary's Hospital, London, with the oral administration of erythromycin and of tetracycline hydrochloride in 120 previously untreated cases of non-gonococcal urethritis are compared. Erythromycin in a total dosage of 6 g. (300 mg. 4 times daily for 5 days) was given to 62 patients, and tetracycline hydrochloride to a total of 6 g. (250 mg. 4 times daily for 6 days) to 58 patients. In assessing the results all cases in which suspected reinfection occurred within 3 months of the conclusion of treatment were classed as failures, and those which were reinfected after 3 months were excluded. With erythromycin the over-all failure rate at 2 to 3 months was 22·8% of those followed up, the corresponding rate with tetracycline being 17·3%. The cumulative failure rates, allowing for differences in follow-up, were 33·9% in cases treated with erythromycin and 29·8% in those given tetracycline. These are compared with a cumulative failure rate of 25·5% after a similar dosage of oxytetracycline or of aureomycin, as reported previously by the authors (*Brit. J. vener. Dis.*, 1955, **31**, 89; *Abstracts of World Medicine*, 1956, **19**, 24). In discussing the failures the author notes the apparent relationship between failure rate and the duration of symptoms before treatment, as shown by the rather better response of patients whose symptoms had been present for more than one week before. Side-effects were few and relatively insignificant. *A. J. Gill*

887. **A Study of the Allergic Reactions to 24,854 Injections of Penicillin and of the Value of the Latter in the Prevention of Syphilis and Gonorrhoea.** (Un estudio de las reacciones alérgicas a la penicilina en 24,854 inyecciones y del valor profiláctico de ellas en la prevención de la sífilis y gonorrea)
R. D. FÁBREGA. *Archivos médicos panameños* [*Arch. méd. panameñ.*] **4**. 65–70, April–June, 1955 [received Nov., 1955]. 5 refs.

The author has studied a group of prostitutes who received prophylactic injections of penicillin at the Social Hygiene Dispensary, Panama City, during the 20-month period between September, 1952, and April, 1954, each woman receiving 600,000 units of P.A.M. weekly (later reduced to 300,000) in a single intramuscular injection; in all 24,854 prophylactic injections were given. The number of allergic reactions occurring in the first 5 months of the study was compared with those in the last 5 months. During these periods the average weekly attendances were 250 and 310 respectively, and numbers of allergic reactions 134 and 34 respectively. From his calculations [of doubtful validity] and on the assumption that no additional allergic reactions occurred in the intervening 10 months [for which no details are given] the author concludes that allergic reactions occur in between 9% and 11% of patients and after 0·6% of injections. When reactions did occur they were controlled by the administration of antihistamines and in no case did the prophylactic injections of penicillin have to be suspended. The commonest reactions were urticaria, headache, and generalized pruritis.

It was noted incidentally that in a group of 182 women 115 pregnancies occurred in the first year of prophylactic injections, as compared with 64 in the previous year. No case of syphilis has occurred in the women receiving prophylactic injections since 1952, the only new cases being in women giving a positive reaction to standard syphilis tests when they became prostitutes. In no instance was the gonococcus found in urethral smears from cases of gonorrhoea [presumably non-specific urethritis] occurring among the frequenters of the brothels concerned.

[The value of this study is reduced by the method of presentation and the results may not represent the true incidence of allergic reactions. But it is clear that weekly injections of P.A.M. may be given over a long period without major ill effect.] *Eric Dunlop*

888. **The Male Gonorrhoea "Carrier". Report of Seven Cases**
J. B. BITTINER and G. O. HORNE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 155–159, Sept., 1955. 2 refs.

The authors point out that relatively little attention has been paid to the symptomless male "carrier" of gonorrhoea, especially since the end of the sulphonamide era, although during it, mainly as a result of inadequate treatment, such cases were well known. They then describe 7 cases of the male carrier state seen at the General Infirmary at Leeds in the last 5 years. In 3 cases the patients admitted previous genito-urinary symptoms, but all were symptomless at their first attendance; none of them had had previous treatment. In 2 cases there was slight urethral discharge after "stripping" of the urethra, but in none was there any evidence of complications. In 5 cases gonococci were found on microscopical examination and/or on culture of urethral scrapings, although in only one of these cases was there any urethral discharge. Gonococci were found in a pus thread from the urine in another case. In 5 cases culture of the prostatic bead gave a positive result, this finding in one case being the only evidence of gonorrhoea. The limited value of the gonococcal complement-fixation test, which was performed in 3 cases, was demonstrated, the result being negative in one case and doubtfully positive in the other 2.

Because of the variation in the findings, treatment with penicillin varied between 300,000 units of a procaine

preparation to 3·6 mega units of a combined procaine–crystalline preparation. There has been no evidence of relapse in any of the 7 cases. The authors point out that if such cases are to be detected the investigations may have to be elaborate, and a high standard of technique, especially in the culturing of the gonococcus, is essential. While the importance of these cases should not be overrated, the possibility that they may be contributing to the reservoir of infection, especially in areas where the falling incidence of gonorrhoea lags behind the general fall, should not be overlooked.

R. S. Morton

889. **Intramuscular Tetracycline (Achromycin) in the Treatment of Acute Gonorrhoea in the Male**
M. MARMELL and A. PRIGOT. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 188–189, Sept., 1955. 3 refs.

In view of the possible misuse of unsupervised oral treatment of gonorrhoea by out-patients and the occurrence of occasional cases of allergic reaction to penicillin the authors have investigated the possibility of a simple alternative parenteral therapy. With this end in view 88 cases of gonorrhoea in males seen at Harlem Hospital, New York, were treated with tetracycline ("achromycin") given intramuscularly into the upper outer quadrant of the buttock. Follow-up was possible in only 45 cases, of which 6 received a single injection of 100 mg. of the antibiotic, 6 were given 200 mg. at one attendance, and 33 cases received 400 mg. each (200 mg. daily on 2 successive days).

Patients given doses of 100 and 200 mg. showed a failure rate of 100%, but of the 33 given 400 mg. over 2 days 28 were cured, a rate of 85%. About two-fifths of those treated complained of local pain at the site of injection lasting up to 48 hours in some cases, and there was one case of allergic reaction, which, however, was not severe, in a patient who had previously manifested a similar reaction to penicillin. The authors conclude that intramuscular tetracycline is effective in the treatment of gonorrhoea and that 400 mg. is the smallest dose that should be used.

[No mention is made in this paper of streptomycin which is already a satisfactory parenteral alternative to penicillin. Follow-up observation consisted in post-treatment examination of a smear and culture of urethral discharge, and its duration of "not shorter than 7 days" is inadequate by most standards.] *A. J. Gill*

890. **Treatment of Gonorrhoea with Intramuscular Tetracycline**
H. A. PERKINS, R. A. KOCH, G. GARA, W. W. STEPHENS, and W. D. DAVID. *Antibiotic Medicine* [*Antibiot. Med.*] 1, 504–506, Sept., 1955. 2 refs.

At the San Francisco City Public Health Clinic 87 patients with acute gonorrhoea were treated with from 1 to 6 intramuscular injections each of 200 mg. of tetracycline given at intervals of 12 to 24 hours. As 17 of these patients failed to return after the first injection and 2 had subsequently to be given penicillin because of side-reactions to tetracycline, this left 68 patients who returned for one re-examination and urethral culture, of whom 36 were also seen on a second occasion.

Out of 15 cases given one injection there were 10 failures, and out of 12 given two injections there were 7 failures, but there were no failures among the 41 patients receiving from 3 to 6 injections.

However, an extreme degree of local discomfort followed the injections and it is not considered that tetracycline given intramuscularly will, in its present form, replace penicillin in the treatment of gonorrhoea.

R. R. Willcox

891. **A Study of Acquired Childhood Syphilis in Madras**
R. V. RAJAM, P. N. RANGIAH, and C. N. SOWMINI. *Indian Journal of Dermatology and Venereology* [*Indian J. Derm. Venereol.*] **21**, 117–129, July–Sept., 1955 [received Nov., 1955). 6 figs., 8 refs.

A detailed study is presented of acquired syphilis in childhood, 385 cases of which were seen over the 7-year period 1948 to 1954 at the Government General Hospital, Madras. In 69% of the cases the source of the infection was familial; the authors state that it was not uncommon in a single family to find inherited syphilis in an infant and non-venereal acquired syphilis in older children. The lesions were usually on the skin and mucous membranes of the mouth and anogenital regions; the primary chancre was seldom observed. The health of the children did not appear to suffer much, and bone lesions were rare. The late lesions were benign and no evidence of involvement of the cardiovascular or nervous system was found in any of the cases in the series. The condition responded rapidly to treatment with penicillin.

[This paper will prove of interest mainly to those concerned with the treatment of the treponematoses in the tropics, although cases of acquired syphilis in childhood are occasionally seen in Britain.] *Robert Lees*

892. **Studies on the Reproducibility and Specificity of the Treponemal Immobilization Test**
P. J. L. SEQUEIRA and A. E. WILKINSON. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 134–142, Sept., 1955. 9 figs., 12 refs.

Of 1,043 treponemal immobilization tests performed on serum from consecutive patients seen at the London and Royal Free Hospitals, London, valid results were obtained in 1,000, the remaining specimens being anti-complementary, toxic to treponemes, or infected. Of the 1,000 valid reactions only 22 were doubtful, and of these, 21 were in sera from known treated syphilitics. Repeated tests were made on 240 of the sera and showed complete agreement in 186 (77·5%), only minor disagreement in 52 (21·6%), and slightly greater disagreement in 2. These results are comparable with the reproducibility obtained in the performance of the conventional serum tests for syphilis.

Sera from 771 presumably non-syphilitic individuals were also examined and the results added to other series reported in the literature, giving a total of 1,868 patients finally presumed to be non-syphilitic; of these, 4 (0·21%) gave a positive reaction and 2 (0·11%) a doubtful reaction. In none of these cases could syphilis be absolutely

excluded. Data are presented of patients, both treated and untreated syphilitics, in whom a standard serum test for syphilis was negative and the treponemal immobilization test positive. Such an event occurs in late and latent syphilis, especially in syphilis of the nervous system. *R. R. Willcox*

893. **Diagnosis of Syphilitic Cardiovascular Disease with Special Reference to Treponemal Immobilization Tests**

B. FRIEDMAN and S. OLANSKY. *American Heart Journal* [*Amer. Heart J.*] **50**, 323–330, Sept., 1955. 6 refs.

Though it is well known that undoubted late manifestations of cardiovascular syphilis sometimes occur in patients whose blood fails to give positive reactions to the usual serological tests, it sometimes happens that it is difficult to diagnose this condition in the absence of collateral evidence of syphilitic infection.

The present report deals with the results of the treponemal immobilization (T.P.I.) test on sera from 33 patients with lesions of the aorta or aortic valves on which the standard serum tests for syphilis (S.T.S.) gave either negative or only weakly positive reactions. The cases were classified on the basis of the history and the clinical impression after examination as (1) syphilitic, (2) non-syphilitic, and (3) due to an unknown or uncertain cause. The results of testing were as follows.

Aetiology	No. of Cases	S.T.S.		T.P.I. Test	
		Negative	Doubtful	Positive	Negative
Syphilitic	12	9	3	9	3
Non-syphilitic	12	12	0	0	12
Uncertain	9	8	1	4	5

(It is interesting to note that treponemal immobilizing antibodies were detected in the blood of patients with cardiovascular syphilis 26 to 43 years after the original infection although the S.T.S. gave negative results.)

The authors [rightly] conclude that the T.P.I. test is of definite help in establishing the existence of syphilis in patients with negative S.T.S. reactions.

G. L. M. McElligott

894. **Benzathine Penicillin in the Management of the Treponematoses**

T. GUTHE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 160–174, Sept., 1955. Bibliography.

The author, who is chief of the Venereal Diseases and Treponematoses Section of the World Health Organization, surveys his subject from the international point of view. He first recalls the now almost universal use of penicillin in the treatment of the treponematoses and proceeds to a review of the pharmacological, clinical, and epidemiological application of the newer preparations. In particular he deals with procaine penicillin with aluminium monostearate (P.A.M.) and benzathine penicillin (dibenzylethylenediamine di(benzylpenicillin)) and their advantages and limitations. The main limitations of the latter are its instability in tropical conditions since the preparation is water-soluble, and its unsuitability for administration by medical auxiliaries working under primitive conditions in carrying out mass campaigns.

Epidemiological indications for antibiotic therapy are discussed from a wide point of view, prophylactic, abortive, and protective treatment being each defined. The important literature concerning preventive treatment with penicillin in venereal syphilis and gonorrhoea is briefly reviewed. The author claims that adequate dosage in the treatment of gonorrhoea does not "mask" syphilis but prevents it. In this regard benzathine penicillin is four times more effective than P.A.M. He points out that preventive treatment is now routine practice in some countries, and that an international survey showed venereologists to be in favour of it. One incident is cited from the U.S.A. in which a diagnosis of secondary syphilis led to the detection of 70 other such cases, and 200 additional contacts in the area were given prophylactic treatment as "enough man-power was not available to apply proper follow-up procedures". In the U.S.A. all patients with gonorrhoea are given 0·6 mega units of benzathine penicillin and this is claimed to be adequate for the majority of patients who may be incubating syphilis; a follow-up examination at 4 months is advised. The administration of benzathine penicillin at monthly intervals to prostitutes in an unnamed country is stated to have cut the syphilis attack rate in these women from 13·6% to 3·9% [but it is admitted that the 3·9% represented one case only, so the total numbers were small].

Preventive treatment in non-venereal, endemic treponematoses is next discussed on the level of mass management, campaigns in various parts of the world being cited. In this and other programmes of mass treatment it was only when prophylactic as well as curative doses of penicillin were given that any reduction in the number of cases really occurred. Data on the use of benzathine penicillin in such mass campaigns is still scanty because of the limitations mentioned above, but the author looks forward confidently to its wider use in preference to P.A.M. when more stable pre-suspended preparations of it become available. The prolonged penicillinaemia obtained with benzathine penicillin should prevent relapses in cases of undiagnosed latency, and should go far to abort cases. Lastly, the side-effects of various types of penicillins are reviewed. The greatest risk is sensitization of the host, leading to skin and anaphylactoid reactions. The author is of the opinion that no penicillin salt has any advantage over another in preventing such reactions, but at least benzathine penicillin can be given in smaller dosage, thus making sensitization less likely. On the other hand local reactions are more common with benzathine penicillin, but the author does not consider this a real disadvantage, since in many cases only one injection is necessary, this "one-session treatment" being an added advantage of benzathine penicillin over other penicillin preparations. The author concludes that considering the enormous amount of penicillin used annually—world production in 1954 was estimated at 500 tons (500,000 kg.)—the incidence of untoward reactions is remarkably low. *R. S. Morton*

Tropical Medicine

895. **The Antimalarial Action of Primaquine against the Blood and Tissue Stages of Falciparum Malaria (Panama, P-F-6 Strain)**
J. ARNOLD, A. S. ALVING, R. S. HOCKWALD, C. B. CLAYMAN, R. J. DERN, E. BEUTLER, C. L. FLANAGAN, and G. M. JEFFERY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 391–397, Sept., 1955. 4 figs., 7 refs.

The authors, at the University of Chicago, have continued their study of the action of primaquine (*J. Lab. clin. Med.*, 1954, **44**, 429; *Abstracts of World Medicine*, 1955, **17**, 196) by examining its effect upon the pre-erythrocytic stages of *Plasmodium falciparum* (P–F-6 strain) in experimentally infected human volunteers. When 8 daily doses of 30 mg. of primaquine base were given to 5 non-immune volunteers, beginning on the day before infection by mosquitoes, all were protected, thus showing that the drug was a true "causal prophylactic". Subinoculation of quantities of 100 to 500 ml. of blood taken from men bitten by infected mosquitoes 5 or 6 days previously showed that no parasites entered the blood stream before the 7th day.

Single doses of 10, 15, 30, or 45 mg. of primaquine base were then given to groups of 4 men during the "prepatent" period, 1, 3, or 5 days after infection with sporozoites. Treatment with 30 or 45 mg. was highly effective when given on the 1st or 3rd day after inoculation, but all doses were ineffective on the 5th day. The dose–response curves indicate that the susceptibility of the tissue forms of the parasite was changing throughout the incubation period. Maximum susceptibility was reached on the 3rd day, but by the 5th day the parasites had become resistant.

Asexual parasites in the circulation were not greatly affected by repeated daily doses of primaquine given to 6 volunteers, and it was necessary to terminate the infection with chloroquine.

It is concluded that primaquine is an effective "causal prophylactic", but that, like other 8-aminoquinoline compounds, it is of little value for the control of parasitaemia in non-immune subjects. *L. G. Goodwin*

896. **Treatment of Malaria with Single Doses of Mepacrine, Chloroquine and Amodiaquin**
C. BORODA. *West African Medical Journal* [*W. Afr. med. J.*] **4**, 144–148, Sept., 1955. 21 refs.

The relative efficacy of mepacrine, chloroquine, and camoquin ("amodiaquin") given in single doses in the treatment of malaria has been studied in 658 adult African labourers on an oil-palm plantation in the British Cameroons. Malaria is endemic in the area, and the adult population can be regarded as partially immune. All the infections in this series of cases were due to *Plasmodium falciparum*. In each case the clinical condition was assessed and blood was examined for the presence of parasites on the first day of treatment. The author states that patients were treated "seriatim, without selection" with one of the three drugs, the doses being mepacrine 474 mg. base, chloroquine 600 mg. base, and camoquin 200 mg. base. The day after the drug was given the patient was reexamined, and if parasites were still present in the blood or the clinical condition was unchanged the treatment was repeated. In none of the cases was it necessary to repeat the treatment on more than 2 successive days—that is, beyond the third day. A single dose of camoquin was more effective in clearing the blood of parasites and achieving clinical cure than either mepacrine or chloroquine. One day's treatment only was required by 55% of the patients receiving camoquin, compared with 51% of those given chloroquine and 35% of those given mepacrine.
William Hughes

897. **Urinary Bilharziasis in European School Children in Southern Rhodesia**
I. BENNIE and D. M. BLAIR. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **49**, 424–434, Sept., 1955. 3 refs.

An investigation into the incidence of urinary bilharziasis in children attending schools in, and within 50 miles of, Salisbury, Rhodesia, is reported, the period of the investigation covering the first two terms of the 1954 school year, when specimens of urine from 10,019 children (5,327 boys and 4,692 girls) were examined for the presence of *Schistosoma* spp. To ensure maximum egg production mild exercises were performed for 5 minutes before urine was passed and, so far as possible, the sample for examination was taken from the vestigial dregs expressed by muscular effort. The specimens were centrifuged before examination, and microscopical findings were checked by hatching miracidia in tubes.

Altogether 425 (4·2%) of the children had *S. haematobium* infection; in 5 cases a double urinary infection was present, when eggs of *S. mansoni* were found as well. The incidence varied in different schools from *nil* to 23%, and, on the whole, was higher in boys (4·8%) than in girls (3·5%). Analysis of the incidence by age groups showed that it ranged from 1·9% in the age group 5 to 7 years to 6·1% in the age group 11 to 15 years. Many of the specimens from children in two schools in which the infection rate was high contained erythrocytes, but no eggs; at a second investigation at these schools, some 8 months after the first, it was found that 17% of the children (boys) had infection with *Schistosoma*. It is suggested that the apparent fall in incidence after the age of 15 is due to the fact that eggs do not easily pass through a bladder mucous membrane already fibrosed by chronic infection. As expected, the incidence was highest in children born in Rhodesia, but it approached the average in immigrants after 2 years' residence. The need for swimming and paddling pools which are free from snails is emphasized. *R. J. Matthews*

Allergy

898. **Acute Diffuse Pneumonia of Asthmatics**
B. FELSON and H. FELSON. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **74**, 235–241, Aug., 1955. 4 figs., 15 refs.

Stating that it is well known that patients who suffer from bronchial asthma are particularly susceptible to attacks of acute pneumonia, the authors describe the abnormal radiological appearances in the lungs in 16 cases of chronic asthma seen at Cincinnati General Hospital, Ohio. These formed two separate radiological patterns, namely, diffuse miliary nodulation and peribronchial infiltration. The appearance of the former resembled miliary tuberculosis; it was bilateral in 6 cases and confined to one lung in 2. The second type (peribronchial infiltration) was present in 11 cases, being bilateral in 10 and showing linear markings, particularly in the region of the hilum of the lung. In 3 cases the pattern changed from one type to the other in successive attacks. The abnormal appearance of the lung fields cleared within a week of symptomatic improvement. Two patients died in an acute attack but no necropsy was performed. In a third who died later necropsy showed nodular foci of acute suppurative bronchiolitis and peribronchiolar lobular pneumonia scattered throughout both lungs. All but 3 of the patients were found to have a raised leucocyte count, with a polymorphonuclear leucocytosis but no eosinophilia. Pathogenic bacteria were cultured from the sputum. All but 2 of the patients were pyrexial on admission. The authors consider that the radiological abnormalities are inflammatory in nature.

[It seems highly probable that the radiological appearances were caused by infection. From the rather inadequate clinical description it appears that few, if any, of these patients were actually suffering from asthma at the time of the acute illness, which must be regarded as an infective condition. There is no reason to believe that it is in any way specific for asthmatics.]

R. S. Bruce Pearson

899. **Pleuro-pulmonary Eosinophilia in Asthmatics. The Pulmonary Forms of Periarteritis Nodosa in Asthma.** (Les pneumo-pleuropathies à cellules éosinophiles des asthmatiques. Les formes pulmonaires de la périartérite noueuse au cours de l'asthme)
J. TURIAF. *Annales de médicine* [*Ann. Méd.*] **56**, 451–495, 1955. 11 figs., bibliography.

The occurrence in asthmatic subjects of areas of pulmonary infiltration associated with attacks of asthma of unaccustomed severity and duration is discussed from the clinical, radiological, histological, and aetiological aspects. In more than 90% of cases the infiltration appears and resolves rapidly, though sometimes complicated by pleural or pleuro-pericardial involvement. Radiological examination is necessary for the demonstration of the lesions, which take various forms: (1) small shadows " the size of a nut ", with a fuzzy outline, commonly in the costophrenic sinus; (2) juxta-hilar shadows which may be very large, resembling a primary tuberculous lesion; (3) subclavicular shadows, usually large and either homogeneous or fluffy, their appearance occasionally suggesting cavitation; and (4) less commonly the infiltration may be miliary and generalized, bronchopneumonic (suggesting neoplastic infiltration), or lobar or multisegmental in distribution. The lesions are often migratory and bilateral, of short duration, changing rapidly and markedly in appearance, and clearing within 2 or 3 weeks without sequelae. The disappearance of the shadows is hastened considerably by treatment with ACTH or cortisone. The recurrent or persistent form of infiltration which makes up the remaining 10% usually occurs in association with severe febrile bouts of asthma and is sometimes accompanied by haemoptysis.

A leucocytosis of 10,000 to 35,000 per c.mm. is found, eosinophil granulocytes always constituting more than 10%, often more than 30%, and not infrequently 50 to 60% of the total. The pleural fluid and sputum also contain large numbers of eosinophils. This eosinophilia is an essential feature of the syndrome and is important in diagnosis. The clinical signs may be misleading, since the picture of severe persistent dyspnoea refractory to anti-asthmatic remedies, together with pyrexia, resembles that of an infective process.

The author suggests that this condition has much in common clinically and histologically with Löffler's syndrome and that the pulmonary infiltrations in these and other allergic conditions may be local manifestations of periarteritis nodosa which, in rare cases, may become generalized. Apart from this eventuality, the condition is benign; its recognition is important chiefly because it may be confused with other, more serious, conditions such as carcinoma, Hodgkin's disease, and tropical eosinophilia.

J. Pepys

900. **The Use of Prednisone in Bronchial Asthma.** (L'impiego del Prednisone nell' asma bronchiale)
U. SERAFINI, A. PIERI, and U. DI NARDO. *Minerva medica* [*Minerva med. (Torino)*] **2**, 22–26, July 4, 1955. 1 fig., 13 refs.

The authors have treated 12 patients with severe bronchial asthma of long duration with prednisone. The drug was given initially in a dose of 30 mg. per day for 2 days, followed by 10 to 15 mg. per day for a further 4 to 16 days. The result was excellent in 7 cases, good in 2, moderate in 2, but there was no effect in one case in which the patient was suffering from severe emphysema. In the patients benefited the improvement in the dyspnoea and cough was noteworthy. The respiratory function was tested by determining the breath-holding time, which was found to be increased in all cases but one. Glycosuria, hypertension, and water retention did not occur.

H. Herxheimer

Nutrition and Metabolism

901. Human Dietary Deficiency of Vitamin B_{12}
F. WOKES, J. BADENOCH, and H. M. SINCLAIR. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **3**, 375–382, Sept.–Oct., 1955. 11 figs., 19 refs.

This paper reports the occurrence of certain symptoms believed to be due to lack of vitamin B_{12} (cyanocobalamin) in a group of British "vegans"—complete vegetarians whose diet contains no food of animal origin whatsoever, thus differing from the usual vegetarian diet, which includes dairy produce. In Dutch and American groups of vegans previously studied such symptoms were much less in evidence, possibly because their average age was greater than that of the group studied by the present authors, which consisted of 32 children and 117 adults, and their adherence to veganism less prolonged. Oral symptoms, especially soreness of the tongue, appeared after about a year of veganism, amenorrhoea and menstrual disorders after about 1½ years, and paraesthesiae after 2 years. Nervous symptoms were also common, but their time of onset could not be fixed. About 20% of the vegans complained of pain and stiffness of the back, amounting in some cases to "poker-back".

The average concentration of vitamin B_{12} in the serum was 111 $\mu\mu$g. per ml. compared with 200 to 360 $\mu\mu$g. per ml. in healthy subjects. The erythrocyte count was slightly subnormal in some subjects, correlation of the values with the serum vitamin-B_{12} levels in these cases giving a curve resembling that found in subacute combined degeneration of the cord rather than in pernicious anaemia. Haemoglobin values were within the normal range, but the mean corpuscular volume was generally above normal. Some evidence was obtained indicating that the concentration of *para*hydroxyphenylpyruvic acid (which is derived from tyrosine, in the metabolism of which vitamin B_{12} may be concerned) in the blood and urine of vegans was higher than in normal subjects. The average urinary excretion of thiocyanate was higher and that of creatinine lower in vegans than in normal subjects. A preliminary study of the children in this group indicates a subnormal rate of growth, whereas the growth and development of vegetarian children do not appear to differ significantly from those of normally fed children living under the same conditions.

H. E. Magee

902. The Role of Vitamin B_{12} in Human Nutrition
F. WOKES and C. W. PICARD. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **3**, 383–390, Sept.–Oct., 1955. 49 refs.

In this paper the authors advance 2 hypotheses to account for the metabolic upsets revealed by examination of the blood and urine of subjects suffering from a dietary deficiency of vitamin B_{12} [see Abstract 901]. One of these postulates a disturbance, caused by lack of the vitamin, in cyanide utilization by the liver, and the other a similar disturbance in the transfer of sulphur for the production of essential amino-acids. These theories are put forward "in the hope of providing a working hypothesis as a basis for discussion and further investigation".

H. E. Magee

903. The Use of C^{14}-Labeled Acetate to Study Cholesterol Metabolism in Man
R. G. GOULD, G. V. LEROY, G. T. OKITA, J. J. KABARA, P. KEEGAN, and D. M. BERGENSTAL. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 372–384, Sept., 1955. 3 figs., 14 refs.

904. Exercise in the Disposition of Dietary Calories. Regulation of Serum Lipoprotein and Cholesterol Levels in Human Subjects
G. V. MANN, K. TEEL, O. HAYES, A. MCNALLY, and D. BRUNO. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 349–355, Sept. 1, 1955. 3 figs., 26 refs.

The authors have investigated the disposition of dietary calories and its effect on the serum lipoprotein and cholesterol levels in 4 young medical students at Harvard School of Public Health, Boston, over four different periods totalling 10 weeks. During Period A (1 week) the subjects ate *ad libitum* (the intakes being carefully noted) and pursued normal activity; the intake of fat ranged from 155 to 175 g. daily and total calories from 2,788 to 3,093 Cal., the dietary fat supplying 50 to 51% of this total. During Period B (4 weeks) the caloric intake was doubled but the fat intake was kept constant at the control level, and the subjects were required to maintain their body weight within 5 lb. (2·27 kg.) of the mean weight during the control period by strenuous daily exercise. During Period C (3 weeks) the subjects returned to the control level of energy expenditure but the high caloric and constant fat intakes were maintained, thus permitting the deposition of body fat. In Period D (2 weeks) the caloric intake was restricted (mean 2,187 Cal.), but the amounts of exercise and dietary fat were kept constant in order to remove the fat deposited in Period C.

In the 3 subjects who completed the whole experiment doubling of the caloric intake did not raise the serum cholesterol or lipoprotein levels during Period B, at which time the subjects were expending the surplus energy by strenuous physical exercise. During Period C, when the high caloric intake was maintained without strenuous exertion, 2 of the 3 subjects gained weight and their serum lipid and lipoprotein levels also rose during this time; in the third subject there was no significant change in serum lipid and lipoprotein levels throughout the experiment, although weight was gained during Period C.

After a lengthy and interesting discussion the authors suggest that the changes observed in the 2 subjects who

gained weight without any increase in serum lipid levels may represent in microcosm the nutritional progress of the average adult American male, consisting in a process of high caloric intake and energy expenditure in youth, followed by decreasing physical activity without any significant reduction in caloric intake in later years, thus leading to increasing body weight, increasing serum lipid and lipoprotein concentration, and the subsequent development of atherosclerosis.

Robert de Mowbray

905. **The Effect of Sitosterol Administration upon the Serum Cholesterol Level and Lipoprotein Pattern**
C. JOYNER and P. T. KUO. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 636–647, Dec., 1955. 8 figs., 20 refs.

906. **Weight Gain from Simple Overeating. I. Character of the Tissue Gained**
A. KEYS, J. T. ANDERSON, and J. BROZEK. *Metabolism* [*Metabolism*] **4**, 427–432, Sept., 1955. 7 refs.

Although the changes in body composition associated with loss of weight from starvation have been studied repeatedly, surprisingly little work has hitherto been carried out on the nature of such changes when weight is gained from overeating. Research on this important subject has now been undertaken by the present authors at the University of Minnesota, Minneapolis, and in this first paper they report the results of an investigation of the changes occurring in 20 men who were induced to overeat for a period of 6 months. These men were stable, cooperative schizophrenics who were otherwise healthy.

Each subject was weighed in air and water at the beginning and end of the period of overeating, and from these figures, after correction for the volume of air in the lungs, the density of the body was calculated. The volume of the extracellular fluid space was estimated from the thiocyanate space by means of a conversion factor of 0·7. Assuming that the mass of bone mineral in the body remained constant, the quantities of extracellular fluid, of fat, and of "cells" gained during the experimental period could then be calculated. Owing to lack of cooperation in the underwater weighings, however, the results in 10 cases were incomplete.

There was a wide variation in weight gain, the average being 10·6 kg., the highest 22·3 kg., and the lowest 2·5 kg. An increase in the extracellular fluid accounted for 17% of the total weight gain in the whole group and for 14% of that in the 10 subjects who were fully investigated. Of the total weight gain in the latter, 61 to 64% (according to the basis of calculation) was made up of fat and about 22% of "cells"—presumably cytoplasm, containing 20% of protein. The composition of the tissues gained appeared to be independent of the total amount of weight gained. The proportion of "cells" in the tissue gained was lower and that of fat higher than in tissue gained by men on refeeding after a prolonged period of undernutrition. The authors conclude from these findings that the "lean body mass" is not absolutely constant in a given individual, the proportions of "cells", extracellular fluid, and bone varying with his nutritional state.

[These results contrast with those of Passmore *et al.* (*Brit. J. Nutr.*, 1955, **9**, 27) who, working on the same problem with different methods, came to the conclusion that the weight gain after overeating was due entirely to deposition of fat and protein, there being no gain of body water.] *A. Gordon Beckett*

907. **Hypertonic Dehydration**
I. W. MACPHEE. *British Medical Journal* [*Brit. med. J.*] **2**, 596–598, Sept. 3, 1955. 6 refs.

In this communication from the University of Liverpool the author describes the condition of hypertonic dehydration, a term used to describe a state in which water and electrolytes are depleted to about the same extent, so that the electrolyte concentration in the body fluid remains near or above normal. This condition is said to be "common, not readily recognized, and but rarely treated" in surgical practice. The patients are often thirsty, and although the peripheral circulation may appear adequate these patients are, the author states, "in a dangerous state, precariously balanced on the edge of peripheral circulatory insufficiency, and are quite unfit to undergo major surgical procedures". The condition can be unmasked by giving the patient a test dose of water; this is retained and the electrolyte concentration falls. Electrolyte replacement can then be accomplished, and the patient made more capable of withstanding operation. These contentions are documented by 2 illustrative case reports.

D. A. K. Black

908. **Complete Relief of Gout**
F. G. W. MARSON. *Lancet* [*Lancet*] **2**, 360–364, Aug. 20, 1955. 3 figs., 9 refs.

The effective control of chronic gouty arthritis in 7 cases treated for long periods with sodium salicylate or with probenecid is reported from the University of Leeds. The cases, selected from a larger series, had been under observation for at least 18 months and in each the blood urea level was normal. No dietary or alcoholic restriction was imposed and apart from a high fluid intake treatment consisted in administration of either sodium salicylate in a dosage of 30 grains (2 g.) three times a day or probenecid in a dosage of 0·5 g. four times a day. Colchicine was given when acute attacks occurred.

In all cases there was relief of chronic symptoms after intervals of 2 to 21 months from the start of treatment, with cessation of pain, reduction in swelling, and healing of ulcers. Acute episodes ceased in all cases, although in one they continued for the first 33 months of treatment. The duration of remission from an acute attack varied between 6 and 43 months. Probenecid, which was given to patients who were sensitive to salicylates, was found less effective as a uricosuric agent than sodium salicylate. In one case it failed to prevent chronic gouty symptoms which had previously been controlled by salicylates, but in others it was of value. The author suggests that it is indicated in patients who cannot tolerate salicylate. *Charles Rolland*

Gastroenterology

909. **Antrenyl—A Clinical Evaluation**
L. J. NOTKIN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **73**, 535–541, Oct. 1, 1955. 33 refs.

The results obtained with oxyphenonium bromide ("antrenyl") in the treatment of 80 ambulatory patients with peptic ulcer and other organic or functional disorders of the gastrointestinal tract are reported from the Jewish General Hospital, Montreal. Of the 80 patients, 69 had previously received standard medical treatment, but only 7 had shown any response. Oxyphenonium bromide was given by mouth in a dosage of 5 mg. 4 times a day, with satisfactory results in 54 of the 80 patients. Side-effects, which were observed in 11 patients, were not troublesome and did not necessitate withdrawal of the drug. In 2 cases (described in detail), in which ileostomy had been performed for ulcerative colitis, administration of oxyphenonium bromide in a dosage of 5 mg. 3 times a day was beneficial, there being an increase in transit time through the small bowel with thickening of the consistency of the faeces.

[The author's findings support the view that oxyphenonium bromide is relatively non-toxic. An objective assessment of the clinical state of the patients before and after treatment would have afforded valuable evidence of the therapeutic efficacy of the drug.]

T. J. Thomson

910. **Chronic Nonspecific Granulomatous Inflammation of the Stomach, Duodenum and Intestine**
A. RICHMAN, H. D. ZEIFER, A. WINKELSTEIN, P. A. KIRSCHNER, and R. D. STEINHARDT. *Gastroenterology* [*Gastroenterology*] **29**, 358–369, Sept., 1955. 4 figs., 16 refs.

The term "non-specific granulomatous inflammation of the stomach and duodenum" is preferred by the authors to regional enteritis because the disease may involve any part of the gastrointestinal tract from the oesophagus to the rectum. The clinical, radiological, and pathological findings in 3 cases seen at the Mount Sinai Hospital, New York, are described. In Case 1, that of a male aged 19 years, the granulomatous inflammation involved the stomach, duodenum, and ileum; in Case 2, that of a male aged 34 years, the stomach, duodenum, ileum, and colon were involved; while in Case 3, that of a boy of 9 years, the involved area included the stomach and the small intestine from the jejunum to the terminal ileum. In Cases 1 and 2 proximal granulomatous inflammation occurred 1½ to 2 years after the onset of distal ileitis. Treatment was by gastro-enterostomy and vagotomy in Case 1, subtotal gastrectomy in Case 2, and gastro-enterostomy with vagotomy followed by administration of cortisone in Case 3.

A review of the clinical picture in these cases and in 14 reported in the literature in which the duodenum and/or stomach were involved with or without more distal disease showed that: (1) distal disease may be followed by proximal disease and vice versa; (2) proximal and distal disease may occur simultaneously (as in Case 3 of the authors' series); and (3) the disease may be limited proximally to the stomach and duodenum with or without jejunal involvement. Histologically there were two distinct patterns: (1) typical granulomatous inflammation with fibrosis and infiltrations of plasma cells and giant cells, and (2) gastritis and duodenitis without tubercles, epithelioid cells, or giant cells. These two variants, in the authors' present view, are considered to be different phases of the same disease.

Joseph Parness

911. **Treatment of Oesophageal Varices in Portal Hypertension by Means of Sclerosing Injections**
R. MACBETH. *British Medical Journal* [*Brit. med. J.*] **2**, 877–880, Oct. 8, 1955. 7 figs., 12 refs.

Further experience in the treatment of oesophageal varices in portal hypertension by injection of sclerosing fluid is reported from the University of Oxford. It is pointed out that all three groups of oesophageal veins —intrinsic, extrinsic, and the venae comitantes of the vagal nerves—may be varicose, since they link portal gastric veins with the systemic azygos system. Haemorrhage occurs from the subepithelial veins, which are the only ones at risk. In many cases haematemesis is the only symptom. Treatment must be directed to relief of the varices since the underlying cause of portal hypertension "is incurable". Of the methods of treatment tried, splenectomy results in temporary relief of portal pressure, venous ligation or gastric transection is inefficient as new channels form, and portacaval anastomosis, the most logical method, is not only technically difficult, but carries a high mortality and the anastomosis may thrombose.

In other hands injection of sclerosing fluids has not been uniformly successful, either because unsuitable technique has been employed or it has been attempted in hopeless cases. The injection is given under general anaesthesia with a special, long needle through an oesophagoscope, 3 ml. of 5% sodium morrhuate being injected at 4 or 5 points. Haemorrhage is controlled by a hydrostatic bag left in position for one or two hours. The treatment is repeated every two weeks until no varices remain. Oesophagoscopy is then carried out regularly for the purpose of treating fresh varices, even if no haemorrhage has occurred.

The prognosis is much worse in patients with liver damage than in those without. Of the author's 30 patients 14 had liver damage; of these, 7 lived more than a year, the longest period of survival being 7½ years. Of 16 without liver damage 14 were alive and well after an average of 7 injections, many leading normal lives.

Some very large profuse varices were successfully sclerosed. The author states that splenectomy is a valuable adjuvant to this treatment because the veins are thereby more readily controlled.

M. Meredith Brown

912. **Functional Disturbances of the Upper Swallowing Mechanism**

J. R. LINDSAY. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **64**, 766–776, Sept., 1955. 7 figs., 7 refs.

Functional disturbance of the upper swallowing mechanism is defined as alteration in the mechanism of swallowing not due to alteration in anatomical structure, and may arise from muscular or nervous changes or disturbance of psychic control. Muscle changes include myasthenia, diffuse sclerosis, scleroderma, and dermatomyositis. There may be asthenia in advanced senility. Nerve changes causing disturbance of mechanism include peripheral neuritis, various forms of paralysis at the jugular foramen, and lesions affecting the nerves as they leave the bulb, such as meningitis, tumours, and fractures of the base of the skull. Intracranial lesions such as haemorrhage or embolus, and also tabes, poliomyelitis, disseminated sclerosis, and syringomyelia, may all interfere with nervous control.

Examination by means of *x* rays, using a barium emulsion, must be done with care when the paralysis is severe, because of the danger of aspiration. Unilateral weakness tends to cause a bulge of the pyriform fossa, but sphincter control is not affected. In bilateral paralysis, such as that from poliomyelitis and tabes, the sphincter may be weak. Spasm of the pharyngeal muscles may occur in tetanus or brain injury, as well as in acute local infection. Dysphagia due to psychological causes cannot be shown radiologically. Endoscopic examination may be of value in revealing malignant disease not otherwise detectable. *William McKenzie*

STOMACH AND DUODENUM

913. **An Analysis of the Results of Conservative Peptic Ulcer Therapy**

T. G. MILLER and D. BERKOWITZ. *Gastroenterology* [*Gastroenterology*] **29**, 353–357, Sept., 1955. 1 fig.

Routine medical treatment of peptic ulcer was carried out in 729 patients at the Hospital of the University of Pennsylvania and 300 patients seen in private practice, all the patients having duodenal ulcer except 30 of the private patients in whom gastric ulcer was present. The regimen consisted in three regular meals daily of non-irritating food, " with intermediate feedings at mid-morning, mid-afternoon, and evening ". Occasionally food was required at night, but more frequent meals were rarely advised. Antacids were prescribed only when the symptoms were not relieved by food alone, and were not continued longer than was necessary for the relief of distress. Antispasmodic and antisecretory drugs of various types were experimented with, mostly in the hospital patients, and sedatives were given fairly frequently, but drug therapy was always withdrawn as soon as this was possible. A stay in hospital was advised only if there were complications or operation was indicated because there was evidence of perforation, haemorrhage, or persistent obstruction. The patients in both groups were followed up for 4 to 15 years (average 9 years), and patients operated on were observed on the average for 7½ years.

The results were considered satisfactory if the patient remained symptom-free or was sufficiently improved to lead a normal life. Medical treatment alone was satisfactory in 45·4% of the hospital patients and in 55·6% of the private patients. Of the 132 private patients who were not improved by medical treatment, 117 came to operation compared with 141 out of 398 hospital patients. When the results of medical treatment and surgery were combined it was found that 62·3% of the hospital patients and 92·3% of the private patients had obtained satisfactory relief, the higher percentage in the latter group being attributed to continued supervision by a single physician and more cooperation on the part of the patient. *Joseph Parness*

914. **Treatment of Peptic Ulcers with " Roter " Tablets**

R. R. HAMILTON. *British Medical Journal* [*Brit. med. J.*] **2**, 827–829, Oct. 1, 1955. 11 refs.

" Roter " tablets contain heavy magnesium carbonate (400 mg.), sodium bicarbonate (200 mg.), calamus (25 mg.), frangula, and bismuth subnitrate (350 mg.) and are intended for use in the treatment of cases of peptic ulceration.

The present author, in general practice, treated 98 patients, 79 with proved and 19 with " presumptive " peptic ulcers, with tablets prepared [not by the original manufacturers] according to the published formula, but differing in appearance from the commercial product and given in smaller doses than those recommended for the latter. Of the 98 patients, 93 were ambulant throughout the period of treatment [but it is not stated whether they were working].

After one month's treatment 81% were free from all symptoms and 9% from the majority of symptoms. In 75% of cases the patient found the tablets superior to alkaline powders. No control subjects were studied, but of 43 patients whose treatment was stopped after 3 months, 57% had relapsed by the end of a year, while among 15 patients with an average duration of symptoms of 10 years who were treated continuously for a year the average number of relapses (a return of even mild symptoms constituting a " relapse ") during that period was 0·73 compared with 4 during the previous year. No evidence of methaemoglobinaemia, which is the main toxic effect of bismuth subnitrate, was found. Two patients complained of headaches, and 3 of diarrhoea, which was severe in one case only. It is concluded that " the treatment is ideal for general practice ".

[These findings need confirmation, as there would seem to be reason for doubt as to the activity of the ulcers in some cases.] *W. A. Bourne*

915. **Hiatus Hernia with Adenocarcinoma Arising in the Region of the Cardia**
J. N. PATTINSON, G. OSBORNE, and B. C. MORSON. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] 7, 90–101, Oct., 1955. 9 figs., 44 refs.

The authors review 109 cases of malignant disease of the lower oesophagus or stomach associated with hiatus hernia which have been reported in the literature and briefly describe 9 such cases seen at the Middlesex Hospital, London, during 1948–53. [The case details are not tabulated and there is no mention of the total number of cases of gastric carcinoma seen during the same period.] In the first 5 cases failure to recognize the condition from the clinical and radiological findings led to delay in treatment until the growth was more or less inoperable. In subsequent cases there was no such delay and radical operation was apparently possible [but there is no mention of the subsequent course]. Six of the patients were women aged 51 to 69, and 3 were men aged 58 to 72. In one case epigastric pain for 9 months was followed by dysphagia; in the others the presenting symptom was dysphagia, which in 6 cases had been present for less than 6 months. In the remaining 3 cases there had been dysphagia for 1, 2, and 9 years respectively.

[This last case is the only one in which the evidence of a large antecedent hiatal hernia seems unequivocal. An infiltrating carcinoma in the region of the cardia may abolish the oesophago-gastric angle and produce a hiatal hernia, and there is no way of knowing how often this happens. The histories of most of these patients and the radiographs reproduced suggest that this possibility should have been taken into account.]

Denys Jennings

916. **Early Post-cibal Symptoms following Gastrectomy. Aetiological Factors, Treatment and Prevention**
W. M. CAPPER and R. B. WELBOURN. *British Journal of Surgery* [*Brit. J. Surg.*] **43**, 24–35, July, 1955. 1 fig., bibliography.

This paper on post-cibal symptoms following gastrectomy is based on the replies to a questionary sent to 50 British physicians and surgeons particularly interested in the subject, on recent literature, and on the authors' own experience. In spite of apparent differences of opinion over many of the problems involved, the authors find general agreement on most of the following points.

There are two main types of post-cibal disturbance following gastrectomy—the "dumping" syndrome and bilious vomiting. Generally, symptoms improve up to 18 months after the operation. Age, the site of ulceration, and the extent of resection do not appear to influence the incidence of symptoms. Patients with very large and active ulcers fare better than those with small ulcers, and men fare better than women. The only technical factor on which there is general agreement concerns the site of the anastomosis. Gastro-duodenal anastomosis is followed by fewer symptoms than is gastro-jejunal; however, ulcers tend to recur more frequently after the Billroth-I type of operation than after other types of gastro-jejunal anastomosis.

Medical treatment is effective in most cases. The recumbent position for half an hour before meals relieves bilious vomiting, while the same position during, or for half an hour after, meals relieves dumping. Foods should be taken as dry as possible, very sweet substances being avoided. Some workers have found paravertebral sympathetic nerve block to be of value, but this finding awaits general confirmation. Of the many surgical procedures carried out for the relief of symptoms entero-enterostomy, the "pantaloon" operation, and jejunal or colonic replacement are not universally favoured; moreover, the recurrence rate of ulceration is believed to be high after these operations. Suture of the lesser curve of the stomach and afferent loop to the left gastric bundle has relieved symptoms in some cases.

The most effective procedure at the present time is to convert the gastrectomy into a Billroth-I type of anastomosis and, in order to reduce the risk of recurrent ulceration, to perform vagotomy simultaneously.

A. G. Parks

LIVER

917. **Distinctive Nail Changes in Advanced Hepatic Cirrhosis**
D. A. J. MOREY and J. O. BURKE. *Gastroenterology* [*Gastroenterology*] **29**, 258–261, Aug., 1955. 2 figs., 3 refs.

With reference to the description by Terry (*Lancet*, 1954, **1**, 757; *Abstracts of World Medicine*, 1954, **16**, 207) of whiteness of the finger nails in association with cirrhosis of the liver, 4 cases of advanced cirrhosis are described in which extensive opacity of the nail beds occurred. The whiteness extended well up the nail, ending in a sharply defined border with a central peak. In one case the changes were also present in the toe nails. The authors failed to find similar changes in the finger nails of numerous patients suffering from other diseases, acute or chronic.

Thomas Hunt

918. **Hepatic Coma: A Clinical and Pathologic Study**
W. T. FOULK, H. R. BUTT, M. H. STAUFFER, A. H. BAGGENSTOSS, and J. B. GROSS. *Gastroenterology* [*Gastroenterology*] **29**, 171–183, Aug., 1955. 26 refs.

This paper presents an analysis of the clinical and laboratory findings in 52 consecutive cases of hepatic coma seen at the Mayo Clinic, of which 23 were due to cirrhosis, 9 to hepatitis, and the remainder to biliary obstruction or hepatic neoplasm or abscess; necropsy was performed in 44 cases. Although the authors urge that an optimistic outlook be adopted in treatment, only 5 patients recovered. The degree of abnormality demonstrated by various hepatic function tests was of little or no help in the detection of impending coma, and there were no distinguishing features in the course of the illness or in the treatment given between fatal and non-fatal cases. The maintenance of a normal serum potassium level appeared to be of importance in treatment, but the various therapeutic measures which are commonly regarded as of value, such as protein hydrolysates, liver extracts, lipotropic agents, and cortisone or ACTH,

failed to influence the prognosis. (The intravenous administration of glutamic acid was not tried.)

Haemorrhage, infection, paracentesis, and surgical procedures seemed to be the most frequent factors precipitating coma, while in a few cases clinical evidence of impending coma apparently disappeared when a diet poor in protein was given. *Thomas Hunt*

INTESTINES

919. **Nutritional and Metabolic Factors in the Aetiology and Treatment of Regional Ileitis**
W. T. COOKE. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **17**, 137–158, Sept., 1955. 10 figs., 43 refs.

With reference to his personal experience of 90 cases of regional ileitis at the Birmingham United Hospitals during the past 12 years the author first discusses the natural history of the disorder. The main features emphasized are: the relatively early age of onset in most cases; the tendency of the disease to be self-limiting provided adequate supporting treatment is maintained sufficiently long to make this possible; the frequency of generalized intestinal involvement, as evidenced by the occurrence of steatorrhoea; and the familial occurrence of the disease.

The author then considers the various functional disabilities which may result from regional ileitis. Of 57 patients in whom fat absorption was investigated, steatorrhoea was present in as many as 45. Recurrence after operation was found to be more frequent among patients with preoperative steatorrhoea than among those without, suggesting that steatorrhoea may be an indication of an extensive functional derangement of the intestine which may not be evident on inspection at operation. Electrolyte depletion, especially loss of potassium, is a most important complication. In the author's earlier cases the serum potassium level was not determined, but an abnormally low level was found in 16 of the later cases. Potassium deficiency may be an important factor in the loss of weight, lassitude, asthenia, anorexia, ileus, and mental disturbances suffered by patients with regional ileitis. A reduction in the serum protein content—supposedly the result of increased faecal loss of organic nitrogen on the one hand, and increased protein catabolism in the presence of grossly deranged fat absorption on the other—was a common finding, but concomitant liver damage was not detected in any of the author's cases. Anaemia was neither frequent nor severe—a few patients had mild iron-deficiency anaemia and 18 had mild macrocytic anaemia, though achlorhydria was not found in any of the patients who were subjected to a test meal. Other evidence of systemic disturbance included as many as 48 cases of finger-clubbing and 34 of glossitis—sometimes transient. Skin lesions suggestive of pellagra were seen in 5 cases, and when the onset of regional ileitis had occurred before puberty the retarding effect on growth was most striking. Other diseases commonly associated with the disorder are pulmonary tuberculosis (3 cases in the author's series), peptic ulceration (11 cases), and mental disturbance (5 cases, apart from 2 cases of mild confusion associated with pellagra). The reason for this last association awaits further clarification.

Treatment should be primarily medical, and surgery undertaken only when specifically indicated by severe obstructive symptoms, intestinal fistulae, distended loops, or failure to thrive after a prolonged period of rest and supportive measures. The ideal time for operation is after the condition has become localized and fibrosed in as small an area as possible. Extensive excision does not appear to prevent recurrence and should be avoided. That treatment with cortisone or ACTH (corticotrophin) may result in symptomatic improvement is not denied, but it is questionable whether it affects the underlying disease process. It is to be doubted whether *x*-ray therapy has any place in treatment at all.

Adrian V. Adams

HERNIA

920. **The Symptoms of Hiatus Hernia**
H. M. LEATHER. *British Medical Journal* [*Brit. med. J.*] **2**, 934–937, Oct. 15, 1955. 2 figs., 11 refs.

The symptomatology of hiatus hernia is discussed with reference to the findings in two groups of patients: (1) 54 patients (21 men and 33 women) seen at the Bristol Royal Infirmary between May, 1952, and October, 1954, in whom *x*-ray examination revealed a hiatus hernia and no other cause for the symptoms was found; and (2) 7 patients with symptoms attributed to heart disease in whom a hiatus hernia was the only detectable abnormality.

Of the 54 patients in Group 1, 46 had "sliding" and 8 had "rolling" herniae. In general, the symptoms were similar to those described by other observers. Heartburn was noted in 40 cases, flatulence in 38, and acid regurgitation in 36. In 42 cases symptoms were aggravated by posture. Pain, usually diffuse, was present in 32 cases [a rather higher proportion than in other reported series]; in 28 of these it was epigastric and in 4 it was felt only on the left side. In about half the cases the pain was unrelated to meals, while in the remainder it came on at varying intervals after meals and was generally aggravated by fatty foods. Vomiting occurred after meals in 20 cases and at night only in 8; in most of the latter group vomiting (often of large quantities) was the presenting symptom. Obesity was a feature in 34 cases. Two cases are described in which there was sudden severe pain in the abdomen and chest following trauma; on investigation a hiatus hernia was the only abnormality present.

In all 7 cases in Group 2 the pain was at first thought to be of anginal origin, the distribution being similar to that in cardiac ischaemia, but a careful investigation revealed that the relationship to exercise was inconstant and that aggravating factors were the taking of food, the horizontal position, and anxiety. In these cases the relief obtained with belladonna and antacids was usually greater than that obtained with nitroglycerin.

T. D. Kellock

Cardiovascular System

921. **Radioiodine Treatment of Euthyroid Cardiac Disease. Four Years of Experience with Two Hundred Thirty-one Patients**
H. L. JAFFE, M. H. ROSENFELD, F. W. POBIRS, and L. J. STUPPY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 434–439, Oct. 1, 1955. 3 figs., 13 refs.

The authors report, from the Cedars of Lebanon Hospital, Los Angeles, the results of the use of radioactive iodine (^{131}I) in the treatment of 231 euthyroid patients who were suffering from angina pectoris, or congestive cardiac failure, or both. (Patients with active rheumatic fever, recent coronary occlusion, or manifest hyper- or hypo-thyroidism were not accepted for treatment.) Of the 231 patients, 100 have been observed for 4 years and 131 for 6 months to 3 years, the average period of follow-up for the whole series being 29 months. The rationale of the treatment is to produce a relatively hypothyroid state which, by lowering the metabolism of the body, will lessen the work of the heart. The authors stress that this therapy is purely symptomatic, and all the other accepted methods of treatment of heart disease were continued. In order to obviate the development of severe hypothyroidism thyroid extract was prescribed when necessary in doses of $\frac{1}{10}$ to $\frac{1}{2}$ grain (6 to 30 mg.) daily, and the patients were instructed to watch for and report early symptoms of hypothyroidism. As a preliminary, first a test dose and then 500 μc. of ^{131}I were administered and the following day a silhouette outline of the thyroid gland (a "thyrogram") was obtained by means of a scintillation counter. This provided, for later comparison, information about the size, shape, and degree of uptake of ^{131}I by the entire thyroid gland. The treatment itself consisted in weekly oral doses of 6 mc. of ^{131}I for 5 weeks. This course was repeated twice at monthly intervals only if at the end of each month further thyrograms and clinical findings indicated insufficient suppression of thyroid activity. The advantages of giving multiple small doses are pointed out. The clinical improvement in each case was assessed in relation to the individual severity of previous symptoms and to the necessity for the use of other therapeutic measures.

Of the 231 cases, the results were considered "excellent" in 53% and "good" in 33%, no improvement being noted in 14%. Patients with angina benefited more than those with congestive cardiac failure or with the combination of failure and angina, although the proportion of "excellent" results was not very different in the three classes (56, 53, and 48% respectively). Patients with angina and failure combined showed, as might be expected, the highest mortality. Of the first 100 patients treated and followed up for 4 years 45% have died. Of the 55 patients in this group in whom the result was adjudged as "excellent" 23 (42%) have died, of 28 with a "good" result 7 (25%) have died, and of 17 with a poor result 15 (88%) have died. The authors point out that this evaluation of results referred to a circumscribed period of time and that while the proportion of deaths was high, the treatment resulted in clinical improvement, often marked, for the duration of the patient's life and is therefore considered worth while. There has been no evidence to suggest that this type of treatment has shortened the duration of life or hastened the development of atherosclerosis in these patients.

Marcel Malden

922. **Levarterenol Bitartrate (Levophed) in the Treatment of Cardiac Arrhythmias**
J. T. MCGINN and J. SCHLUGER. *American Heart Journal* [*Amer. Heart J.*] **50**, 625–633, Oct., 1955. 8 figs., 14 refs.

The authors report, from Long Island College Hospital, Brooklyn, New York, 6 cases in which supraventricular tachycardia was relieved by the administration of L-noradrenaline given intravenously at the rate of 20 to 40 drops per minute of a solution containing 8 to 18 mg. of noradrenaline per litre. The effect of the drug is to increase blood pressure; it is assumed that by this means the vagus nerve is reflexly stimulated and thus causes cardiac slowing. In one case of auricular flutter there was a temporary slowing of the heart rate, but the abnormal rhythm persisted.

H. E. Holling

CONGENITAL HEART DISEASE

923. **The Closure of Atrial Septal Defects under Direct Vision with Hypothermia.** (Der Vorhofseptumdefekt und sein operativer Verschluss unter Sicht des Auges in Unterkühlungsanästhesie)
E. DERRA, O. BAYER, and F. GROSSE-BROCKHOFF. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 1277–1281 and 1295–1296, Sept. 9, 1955. 5 figs., bibliography.

Writing from the Medical Academy, Düsseldorf, the authors express the opinion that atrial septal defect, which occurs as an isolated anomaly in roughly 10% of all cases of congenital heart disease, has often been diagnosed in the past as mitral insufficiency without dilatation of the left auricle. The diagnostic signs and symptoms are discussed and an operation is described, with illustrations, for closure of the defect under direct vision and with hypothermia to 26° C. This permits arrest of the venous return for several minutes without damage to the brain, and secures an essentially bloodless field.

This operation has so far been performed on 8 patients aged between 14 and 42 years. In 2 cases there were anomalous pulmonary veins, while in all cases the bore of the aorta was small in comparison with that of the

pulmonary artery. A striking observation was that, except in the oldest patient, a persistent thymus gland was present in all cases. Ventricular fibrillation occurred during the first operation performed, but was successfully controlled. One patient died of cerebral embolus 12 days after operation, but in the others the post-operative course was relatively uneventful, and at follow-up several months after the operation their condition was markedly improved. Although it was still too early to form any final opinion it was noted that in all cases the size of the heart had diminished, while in 3 cases the associated murmurs had disappeared and in the others were much less audible. The shortness of breath on the least exertion and the limitation of functional capacity which were marked before operation had greatly improved in all but one of the patients.

The authors' indications for the operation are (1) a considerable left-to-right shunt and/or severe symptoms, and (2) severe pulmonary hypertension existing with a conspicuous left-to-right shunt. The presence of anomalous pulmonary veins is not a contraindication if less than half of the veins are transposed. Associated mitral stenosis must be dealt with by the performance of valvotomy before the defect is closed. The authors recommend that the operation should be performed as early in life as possible, as at that time secondary alterations in the pulmonary circulation are better borne than at a later age. In their experience, however, the operation may be undertaken in older patients with a good chance of success, provided that unduly severe pulmonary hypertonia following pulmonary sclerosis is not present. *D. P. McDonald*

CHRONIC VALVULAR DISEASE

924. **Aortic Stenosis: a Clinical Study**
M. B. MATTHEWS, W. E. MEDD, and R. GORLIN. *British Medical Journal* [*Brit. med. J.*] **2**, 759–763, Sept. 24, 1955. 7 figs., 36 refs.

In view of the recently increased scope of surgical treatment of cardiac conditions the authors have carried out a clinical study of 50 consecutive cases of aortic stenosis in 31 men and 19 women attending the out-patient department of St. Thomas's Hospital, London, "with special reference to the features which might determine their suitability for operation". Aetiologically, of the 50 cases, 6 were classed as congenital, 20 as rheumatic, and 24 (21 in males) as indeterminate.

The symptoms are tabulated and briefly discussed. Of the signs, the authors found the anacrotic pulse to be difficult to distinguish, although brachial arterial pulse records almost invariably showed a slow upstroke. In cases in which aortic incompetence was also present, the bisferient pulse could be felt by occluding the brachial artery. The aortic second sound was normal in most cases. No attempt was made to grade the aortic systolic murmur, the authors feeling that its loudness depends on other factors, such as the blood flow, rather than the size of the orifice. Calcification of the valve was seen on screening in 33 of the 50 cases. The natural history of the disease is discussed and compared with that of mitral stenosis. The advantages and disadvantages of early operation are enumerated. It is pointed out that the scanty figures at present available suggest that the operative mortality is high, and the long-term results are unknown. *C. W. C. Bain*

925. **Mitral Valve Disease and Mitral Valvotomy**
J. F. GOODWIN, J. D. HUNTER, W. P. CLELAND, L. G. DAVIES, and R. E. STEINER. *British Medical Journal* [*Brit. med. J.*] **2**, 573–585, Sept. 3, 1955. 18 figs., 38 refs.

The authors give an account of 75 cases of mitral stenosis treated at Hammersmith Hospital (Postgraduate Medical School of London) by mitral valvotomy, with a follow-up of 56 cases for a period of 6 months or over. The clinical assessment and selection of the patients are described in detail, and the various grading systems used in assessing the severity of different symptoms are defined. In addition, the diagnostic value of the signs present in 10 patients in whom mitral incompetence was an associated factor is discussed. The relation between the severity of the four major symptoms—dyspnoea on effort, bronchitis, haemoptysis, and paroxysmal dyspnoea—and the size of the mitral orifice as found at operation is examined, and it is concluded that whereas the degree of dyspnoea of effort is inversely proportional to the size of the orifice, the severity of the remaining three symptoms is not influenced by narrowing beyond a critical diameter of 1·5 cm.

Four patients died shortly after operation and 5 others died after various intervals. Two-thirds of the patients could be said to be subjectively improved after operation, but in only one-half of these was it possible to confirm the improvement objectively. It was found that the best results were generally obtained in those cases with a mobile valve in which a good commissural split could be made, while those in which calcification and incompetence were present were less likely to benefit. The authors draw attention to the slow progress of symptoms in many cases of established mitral disease and suggest that the selection of cases suitable for surgery must be guided by careful clinical and radiological assessment.

[The paper contains a quantity of valuable information and detail which is relevant to the surgery of mitral stenosis.] *T. Holmes Sellors*

926. **The Clinical Indications for Mitral Valvotomy.** (Ueber die klinische Indikationsstellung zur Valvulotomie der Mitralklappe)
E. F. HUEBER, O. STEINHARDT, and H. THALER. *Wiener klinische Wochenschrift* [*Wien. klin. Wschr.*] **67**, 744–749, Sept. 23, 1955. 9 refs.

In this paper from the First Medical and Second Surgical University Clinics, Vienna, the authors discuss the indications for mitral valvotomy in the light of results obtained in 26 cases. They agree with Dexter (*Circulation* (*N.Y.*), 1954, **9**, 758) that none of the recently introduced diagnostic aids, such as cardiac catheterization, radiography, and electrokymography, can alone

give a more reliable index of the severity of mitral stenosis than an accurate clinical examination of the patient. Dexter's grading of his cases and the results obtained by him are described in detail, and the authors' own results in 15 cases of uncomplicated mitral stenosis reported.

The diagnosis of complicating disease simultaneously present in other valves is dealt with at length. Attention is drawn to the fact that the cardinal signs of mitral insufficiency—a systolic murmur and enlarged left ventricle—may also be present with uncomplicated mitral stenosis; associated insufficiency may thus be diagnosed more frequently than it is actually present. The differential diagnosis generally depends upon the relative skill of the observer; as symptoms are very variable, errors are possible and great care must be taken, since associated insufficiency may be the decisive factor in the success or otherwise of the operation. Slight degrees of insufficiency are not of great consequence, but severe degrees are a definite contra-indication. In general, the combination of mitral stenosis with failure of one of the other valves is a contraindication, though tricuspid insufficiency is excepted. Liability to infarction alone is not a contra-indication nor is auricular fibrillation, although its presence indicates that the most favourable time for operation has passed. Pregnancy is not an absolute contraindication, as is shown by 7 successful results in pregnant patients. However, acute or subacute bacterial endocarditis and rheumatic inflammation are absolute contraindications. *D. P. McDonald*

927. **Electrocardiographic Changes during Mitral Commissurotomy**

H. Gross, E. R. Kepes, D. Young, and C. D. Enselberg. *American Heart Journal* [*Amer. Heart J.*] **50**, 373–381, Sept., 1955. 4 figs., 6 refs.

Continuous electrocardiographic records were taken throughout each of the first 100 operations for mitral valvotomy performed at the Montefiore Hospital, New York. In every case irregularities were noted during the course of the operation, the most significant of which were ventricular extrasystoles (in 62), and ventricular paroxysmal tachycardia (in 44), generally of a rather irregular pattern. These usually occurred during active handling of the heart or during valvotomy itself. Other findings included S–T depression, which was apparently related to tachycardia rather than to a fall in arterial oxygen saturation as measured by ear oximeter.

Irregularities usually ceased spontaneously soon after the essential part of the operation had been completed, although one patient in whom arrhythmia had been induced during intubation died later in a paroxysm of ventricular tachycardia. In 22 cases treatment was thought necessary either because the tachycardia persisted, or because the blood pressure fell. Procainamide was effective in controlling ventricular tachycardia but not other types, quinidine usually suppressed frequent extrasystoles, and digitalis controlled the tachycardia accompanying auricular fibrillation. Noradrenaline effectively corrected hypotension. *J. A. Cosh*

928. **Electrocardiographic Study in 75 Cases of Mitral Stenosis before and after Commissurotomy**

O. Giallorето and P. David. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **73**, 380–386, Sept. 1, 1955. 10 refs.

Preoperative electrocardiograms from 75 patients with pure mitral stenosis undergoing commissurotomy were studied at the Institute of Cardiology of Montreal, but postoperative records (mostly made within 2 months of operation) were available in only 59 of these cases. The authors define precisely the standards adopted for the diagnosis of right axis deviation, left and right auricular hypertrophy, and right ventricular hypertrophy in the analysis of these records.

Before operation right axis deviation was present in 46·5% and left deviation in 2·7% (2 cases, in one of which aortic regurgitation subsequently developed, and in the other mitral incompetence), the axis not being deviated in the remainder. After operation deviation to the right was found in 16·9%, to the left in 11·8%, and no deviation in 71·1%. The incidence of isolated right auricular hypertrophy fell after operation from 21·9% to 11·8% and that for combined auricular hypertrophy from 16·4% to 0·7%, whereas the proportion of cases with no sign of hypertrophy increased from 17·8% to 49%. The proportion with auricular fibrillation remained a little over 20%. The proportion of cases with right ventricular hypertrophy fell from 51·3% to 43·8% after operation. No case of complete right bundle-branch block was observed, but incomplete block was present before operation in 11 cases. This disappeared after commissurotomy in 4 cases, but appeared in 5 new cases. The proportion of normal tracings increased from 5·4% before to 22% after operation.

It is concluded that in mitral stenosis "the electrocardiographic signs of auricular hypertrophy are more often signs of dilatation than of irreversible anatomical hypertrophy". *R. S. Stevens*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

929. **The Use of Pentaerythritol Tetranitrate in Chronic Coronary Insufficiency**

H. N. Rosenberg and A. L. Michelson. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 254–258, Sept., 1955. 9 refs.

The effect of pentaerythritol tetranitrate ("peritrate") in doses of 20 or 30 mg. 4 times a day on the severity of anginal pain and the requirement of nitroglycerin tablets for its relief was studied in 20 patients with coronary insufficiency at Boston City Hospital (Boston University). The double-blind technique was employed and the period of observation varied from one to 6 months.

Five patients reported a degree of improvement which could be considered statistically significant, while in 11 cases the patients obtained a favourable general impression of the effect of the drug but their detailed daily reports proved equivocal on closer analysis. A dose of

30 mg. 4 times a day seemed more effective than the smaller dose, but caused side-effects which prevented its continuation in 3 cases. The authors express a favourable if guarded opinion of the value of the drug in the treatment of anginal pain. *A. Schott*

930. **The Treatment of Angina Pectoris with a Nitroglycerin Ointment**
J. A. Davis and B. H. Wiesel. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 259–263, Sept., 1955. 3 refs.

In 17 patients with angina pectoris the effect of the application to the chest of a 2% nitroglycerin ointment (usually an amount containing 8 to 12 mg. applied 3 or 4 times a day over an area 5 to 8 inches (13 to 20 cm.) in diameter) as an adjuvant to the usual treatment was investigated at the Medical College of Alabama, Birmingham, Alabama. A favourable effect was noted in 9 cases, in which the frequency of attacks was reduced. The authors advocate further trial, and warn against sudden withdrawal of the treatment, which appeared in some cases to cause more severe coronary insufficiency or myocardial infarction.

[In view of the small number of cases treated, absence of controls, and largely subjective method of evaluation of results any conclusion as to the value of this treatment cannot be more than tentative.] *A. Schott*

931. **The Heart Muscle and the Electrocardiogram in Coronary Disease. III. A New Classification of Ventricular Myocardial Damage Derived from the Clinicopathologic Findings in 100 Patients**
J. J. Sayen, W. F. Sheldon, and C. C. Wolferth. *Circulation* [*Circulation (N.Y.)*] **12**, 321–337 and 530–542, Sept. and Oct., 1955. 8 figs., 21 refs.

932. **The Anterior Chest Wall Syndrome—Chest Pain Resembling Pain of Cardiac Origin**
M. Prinzmetal and R. A. Massumi. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 177–184, Sept. 17, 1955. 1 fig., 18 refs.

Pain in the anterior chest wall in a middle-aged patient is initially [and properly] regarded as indicating serious heart disease. Such pain is not always of cardiac origin, however, and recognition of the non-cardiac conditions which give rise to the pain is therefore important. The present authors describe a painful somatic affection of the anterior chest wall which they have observed in patients with and without a history of myocardial infarction at the Cedars of Lebanon Hospital, Los Angeles. They claim that the syndrome has not previously been described. The patients were between 30 and 75 years of age, and in a high proportion the syndrome was observed after an attack of coronary occlusion. Presternal pain without radiation developed within 4 to 6 weeks, occasionally several months, after the attack; it was continuous, but exacerbations occurred which were unrelated to exercise. Body movements would at times provoke an acute exacerbation which did not respond to administration of glyceryl trinitrate. The general health of the patients was unaffected, but an anxiety state was frequently observed. The outstanding physical sign was tenderness over the anterior chest wall, especially over the costal cartilages, and pressure over these areas provoked an attack of pain. No trophic or other local changes were observed. Biopsy of the anterior chest wall in cases of short duration showed that the tissue was normal, but in 2 cases in which the condition had been present for 3 years and 7 years respectively muscular degeneration and lymphocytic infiltration were found.

The differential diagnosis is from coronary arterial disease, osteoarthritis of the cervico-dorsal spine, hiatus hernia, diseases of the bone involving the ribs, Tietze's disease, muscular strain, and, in females, painful diseases of the breast. Each of these is discussed in detail.

In treatment short courses of cortisone were strikingly successful, but if there was residual pain *x*-ray therapy was given for a few days, with satisfactory results. Breathing exercises and reassurance of the patient were valuable adjuvants. As the authors emphasize, it is necessary to bear in mind that some of these patients may also be suffering from genuine angina pectoris.

This syndrome, the cause of which is unknown, is believed to be analogous pathogenetically to the shoulder-hand syndrome. *F. Starer*

SYSTEMIC CIRCULATORY DISORDERS

933. **The Neurogenic Component in Hypertension**
A. E. Doyle and F. H. Smirk. *Circulation* [*Circulation (N.Y.)*] **12**, 543–552, Oct., 1955. 4 figs., 14 refs.

The maximum fall in the blood pressure after administration of a ganglion-blocking agent is a measure of the part played by neurogenic control of vascular tone in the maintenance of the blood pressure. It has been suggested that chemical pressor agents enhance the effects of neurogenic vasoconstriction in hypertension. To test this hypothesis the authors, working at the University of Otago, Dunedin, New Zealand, have observed the fall in blood pressure after the administration of hexamethonium to 22 normal subjects and 80 patients suffering from hypertension of various types. Initially 25 mg. of hexamethonium was administered intravenously, further intravenous doses of 15 mg. being given at 2-minute intervals until two successive doses produced no further fall in blood pressure. Observations were made with the patient recumbent, and also with the feet tilted down to 60 degrees; in the latter case smaller doses of hexamethonium were used.

In both positions the fall in blood pressure induced by hexamethonium was greater in hypertensive patients than in normal subjects. The magnitude of the fall was related directly to the initial height of the blood pressure and inversely to the lowest level of blood pressure attained. In a further experiment the blood pressure of 60 patients was raised by the intravenous infusion of "angiotonin", noradrenaline, or *s*-methyl *iso*thiourea. The maximum fall in blood pressure obtained in response to hexamethonium was shown to be less when the blood pressure was first raised by these chemical agents than when no pressor agent was given. In attempting to

explain these results the authors suggest that when a chemical pressor factor is present the blood pressure control mechanism reacts by reducing the neurogenic component. Long exposure to such pressor stimuli is thought to induce the vasomotor centres to exercise their regulating function at a higher than normal level.

Bernard Isaacs

934. **The Effect of Oral 1-Hydrazinophthalazine Therapy on Renal Function in Essential Vascular Hypertension**

I. J. MADER and L. T. ISERI. *American Heart Journal* [*Amer. Heart J.*] **50**, 556–566, Oct., 1955. 6 figs., 16 refs.

At Detroit Receiving Hospital (Wayne University), Detroit, 14 patients with severe hypertension were treated with oral 1-hydrazinophthalazine (" apresoline ") and subcutaneous hexamethonium. From initial doses of 25 mg. and 3 to 5 mg. respectively the dosage was gradually increased to a maximum ranging from 400 to 900 mg. of 1-hydrazinophthalazine and from 20 to 100 mg. of hexamethonium daily. The patients were observed in hospital under controlled conditions, blood pressure being recorded twice daily. Immediately before starting therapy and again 14 to 41 days afterwards the renal clearances of inulin and PAH were measured and from the results the glomerular filtration rate, renal plasma flow, and maximum tubular excretory capacity were calculated. In some cases the cardiac output was measured by cardiac catheterization. In 12 of the patients there was a fall of blood pressure greater than 15 mm. Hg, and in 10 of these the renal studies showed that a decrease in the afferent arteriolar resistance had occurred and that renal plasma flow had increased, although no significant change in cardiac output was observed, indicating a decrease in the renal ischaemia. The duration of the effect is not known.

H. E. Holling

935. **Pentolinium and Hexamethonium Combined with Rauwolfia in the Treatment of Hypertension**

E. DENNIS, R. FORD, R. HERSCHBERGER, and J. H. MOYER. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 597–600, Oct. 6, 1955. 3 refs.

Hexamethonium bromide and pentolinium were each given with rauwolfia in the treatment of hypertension, and the results obtained in the following two groups of patients were compared: Group 1—75 patients who had already received rauwolfia with hexamethonium for 12 to 18 months and whose treatment was changed to rauwolfia combined with pentolinium; Group 2—34 patients who received rauwolfia and pentolinium from the outset. Rauwolfia was given as reserpine (2 mg. daily), or " alseroxylon " (8 mg. daily), or whole root (400 to 500 mg. daily). A fall of 20 mm. Hg or more in the mean blood pressure in the upright position was considered to indicate a response to treatment. The ganglion-blocking drugs were given by a titration method —that is, small doses were administered at first, gradually increasing till optimum reduction in blood pressure was obtained or side-effects prohibited any further increase. Of the 75 patients in Group 1, 57 responded to rauwolfia with hexamethonium and 28 became normotensive. In the same group, 29 responded to rauwolfia combined with pentolinium and 25 became normotensive. It was noted [surprisingly] that 12 patients failed to respond to rauwolfia with hexamethonium but responded when pentolinium replaced hexamethonium, and 10 patients responsive to rauwolfia and hexamethonium failed to respond to rauwolfia and pentolinium. Side-effects occurred with about the same frequency with either combination, but were less intense when pentolinium was given. Of the 34 patients receiving rauwolfia and pentolinium only, 32 responded satisfactorily and 14 became normotensive. The authors state that the average daily dose of hexamethonium for all patients who were responsive was 2·307 mg. compared with 0·341 mg. of pentolinium, suggesting that, milligramme for milligramme, pentolinium is nearly 7 times more potent than hexamethonium.

K. G. Lowe

936. **Peripheral Arteriosclerotic Vascular Disease in Diabetics. Results from Lumbar Sympathectomy and Comparative Analysis with Nondiabetic Patients**

R. E. L. BERRY and C. T. FLOTTE. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **71**, 460–467, Sept., 1955. 7 figs., 16 refs.

The authors compare the results of lumbar sympathectomy for arteriosclerotic disease of the legs in patients with and without diabetes treated at the University of Michigan Hospital during the years 1945 to 1952. Of a total of 275 patients treated, 93 (33·9%) were diabetics, 50 being men and 43 women. Of the non-diabetic patients, 170 were men and 12 women. The age distribution was roughly similar in the two groups. The results are described as " good ", " poor; no amputation ", " amputation ", and " dead ". [These descriptions are not elaborated, but " amputation " appears to mean " major amputation ".]

In the small group of 17 diabetics without tissue necrosis the results of sympathectomy were similar to those obtained in the non-diabetic patients without tissue necrosis, while those in the remaining 76 diabetics with tissue necrosis were almost exactly like those obtained in the non-diabetic group with necrosis. Taking all the diabetics together the amputation rate was 50%, poor results without amputation were obtained in 16%, good results in 31%, and 43% are dead. For the non-diabetics the corresponding figures were 37%, 22%, 36%, and 37%. Among those in both groups who died the average survival period was 25 months. Very few good results were obtained in diabetics over the age of 65. [Evidently individual patients have often been included in more than one sub-group in recording the results, since the figures add up to more than the total number of patients treated in each group, and this is reflected in the percentage values, which in sum exceed 100%.]

The severity and duration of the diabetes and the adequacy of its treatment were also examined in relation to the results of sympathectomy. These factors did not appear to affect the proportion of good results obtained, but amputation was needed more often in those judged to have been inadequately treated than in adequately treated patients.

C. J. Longland

Haematology

937. **Oral Iron Compounds. A Therapeutic Comparison**
D. J. O'Sullivan, P. G. Higgins, and J. F. Wilkinson. *Lancet* [*Lancet*] **2**, 482–485, Sept. 3, 1955. 1 fig., 15 refs.

A therapeutic trial was made of four commonly used oral iron preparations—ferric hydroxide, ferrous sulphate, ferrous succinate, and ferrous gluconate—in doses of 210 mg. of elemental iron given daily to 80 patients. Ferric hydroxide in the small daily dose given was unsatisfactory, but the three other preparations produced almost equal and satisfactory haematological responses. Patients refractory to one oral preparation were refractory to all but responded to parenteral iron. Intolerance was observed after ferrous sulphate in 13%, and after ferrous succinate and gluconate in 4% of patients. Ferrous sulphate is effective in smaller doses (210 mg. daily) than are in general use at present.

The relative costs of treating hypochromic anaemias with these ferrous salts in equivalent dosage are compared. Ferrous sulphate is much cheaper than the others and equally efficacious. It maintains its position as a satisfactory therapeutic agent.—[Authors' summary.]

938. **Thalassaemia in a Scottish Family**
L. G. Israels, H. J. Suderman, and J. Hoogstraten. *Lancet* [*Lancet*] **2**, 1318–1320, Dec. 24, 1955. 23 refs.

939. **Studies in Mediterranean (Cooley's) Anemia. II. The Suppression of Hematopoiesis by Transfusions**
C. H. Smith, I. Schulman, R. E. Ando, and G. Stern. *Blood* [*Blood*] **10**, 707–717, July, 1955. 5 figs., 14 refs.

One of the puzzling features of Cooley's anaemia is that even when the spleen has been removed the anticipated rise in the haemoglobin level is not obtained from transfusion of a particular volume of blood. At the New York Hospital–Cornell Medical Center the suppressive effect of transfusion on erythropoiesis and haemoglobin synthesis was studied in 2 patients—one with Cooley's anaemia and one with Cooley's anaemia and sickle-cell disease. By simultaneous determination of haemoglobin concentration, total blood volume, total erythrocyte volume, and survival of transfused erythrocytes, it was possible to distinguish between the circulating haemoglobin and the erythrocyte volumes of donor and recipient. Retardation of endogenous erythropoiesis and haemoglobin synthesis were most marked 1 to 2 weeks after transfusion, the erythrocyte volume in the recipient having fallen 26·5% and the haemoglobin mass 17·5% below the baseline level. Thereafter the retardation became less marked but persisted until the transfused cells had been eliminated. There was no evidence of increased blood destruction. From these observations it was evident that owing to plasma volume shifts, peripheral blood values were not accurate indicators of haematopoietic status in patients with chronic anaemia. The depression of haematopoiesis occurred when the blood values " did not approach normal, let alone polycythaemia ". *E. G. Rees*

940. **The Chemotherapy of Leukaemia with Three New Agents: Demecolcin, Thiocolchicin, and Myleran.** (Essais de chimiothérapie de la leucémie myéloïde par 3 corps nouveaux: démécolcine, thiocolchicine, myleran)
J. Bousser and D. Christol. *Presse médicale* [*Presse méd.*] **63**, 1229–1231, Sept. 21, 1955. 25 refs.

In testing " demecolcin " and " thiocolchicin ", both derivatives of colchicine, at the Hôtel-Dieu, Paris, the authors found that the remissions obtained in the treatment of chronic myeloid leukaemia were transitory. In their opinion the liability of both drugs to produce unpleasant side-effects outweighed any benefit that might be obtained from their use. With " myleran " (1:4-dimethanesulphonyloxybutane), on the other hand, excellent results were obtained in chronic cases with doses of 4 to 8 mg. daily for 1 to 2 months, subsequent maintenance dosage being 2 mg. every 1, 2, or 3 days; no untoward side-effects were noted. In most cases there was a lag period of some 2 to 3 weeks after starting treatment before a decrease in the leucocyte count was seen. The drug had the same beneficial effect in old, previously treated cases, as in new, untreated cases.

In one case of acute myeloblastic relapse of chronic myeloid leukaemia treatment with myleran was started too late and the patient died; in another similar case the blood picture returned to normal but the spleen remained enlarged. In 2 cases of myeloid splenomegaly with myelosclerosis treatment with the drug had no effect on the size of the spleen.

In the authors' opinion the remissions obtained with myleran are of shorter duration than those following radiotherapy; they conclude nevertheless that the drug has much to commend it, since it is cheap and, unlike radiotherapy, requires no elaborate apparatus for its administration. *I. M. Rollo*

941. **The Dimethanesulphonyl Oxides in the Treatment of Chronic Myeloid Leukaemia.** (I dimetansulfonilossidi e la terapia della mielosi leucemica cronica)
G. Consoli and V. M. Napoli. *Riforma medica* [*Rif. med.*] **69**, 929–938, Aug. 20, 1955. 4 figs., bibliography.

The authors report from the University Institute of Special Pathology, Naples, that in 4 cases of chronic myeloid leukaemia which were treated with a total of 200 to 250 mg. of 1:4-dimethylsulphonoxybutane given in doses of 10 to 15 mg. daily the clinical and haematological results were satisfactory, and in agreement with those of other authors. They conclude that this substance exerts a selective cytostatic action on the cells of chronic myelogenous leukaemia and that it is the drug of choice in such cases. *G. Calcutt*

Respiratory System

942. **Developmental Defects in the Lungs**
P. JONES. *Thorax* [*Thorax*] **10**, 205–213, Sept., 1955. 14 figs., 10 refs.

The author reports 19 cases of congenital defect of the lung which were selected for their particular interest from a series of 37 such cases, all treated by the same surgeon since 1939. The abnormalities present, which were multiple in most cases, were of three types, in all of which there was dissociation of the bronchial or pulmonary tissue from the tracheo-bronchial tree, resulting in the formation of cysts at different sites, as follows. (1) *Paratracheal Cysts*. These are diverticula of respiratory epithelium with investments of muscle and cartilage communicating with the trachea or one of the main bronchi. In 2 cases of cervical origin congenital hemivertebrae were present. (2) *Bronchial Cysts*. These were associated in 5 cases with a defect in the pericardium. (3) *Dissociated Lung Cysts* (*Intralobar Sequestration*). These cysts receive their blood supply from the systemic circulation through aberrant vessels arising directly from the aorta or an intercostal artery.

The defect leading to development of dissociated lung segments is thought to be primarily vascular, hyperplasia of an element of the systemic circulation occurring secondarily as a compensatory mechanism where a portion of the pulmonary circulation has failed to develop. *A. M. Rackow*

943. **Congenital Pulmonary Agenesis**
L. A. HOCHBERG and E. A. NACLERIO. *Diseases of the Chest* [*Dis. Chest*] **28**, 275–281, Sept., 1955. 4 figs., 29 refs.

944. **Chronic Pulmonary Disease in Histoplasmin Reactors. A Review of 229 Cases Discovered through Chest Clinic Examinations**
F. C. WHITE. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 274–296, Sept., 1955. 10 figs., 43 refs.

A total of 229 patients with chronic pulmonary histoplasmosis have been observed, most of them for 5 to 15 years, at the Ray Brook State Tuberculosis Clinics in the north-eastern part of New York State. All gave a positive reaction to the histoplasmin skin test, but only 34 out of the 172 patients tested gave a positive complement-fixation reaction, while *Histoplasma capsulatum* was isolated from the sputum in only 3 cases. About one-third of the patients had radiological evidence of disseminated lung disease, the remainder having single lesions or, more rarely, multiple lesions less widely distributed. The initial symptoms resembled those of influenza and were more severe in disseminated disease, but disappeared in most cases after some 6 weeks. A dry cough at first was followed after 4 to 7 days by expectoration of tenacious white or yellow sputum.

The mottled areas of infiltration seen on the initial radiographs shrank and became nodular after a period varying from one month to over 2 years. Eventually the nodules became spherical or ovoid and, after 3 to 15 years, central calcification appeared. Finally the dense area surrounding the calcification gradually resolved over a period ranging from 6 to over 13 years. Initial hilar enlargement was present in the majority of cases and cleared within a few months. None of the patients died, and in only 7 cases did fresh areas of disease or central cavitation of nodules develop. The disease as seen in this series was therefore essentially mild and self-limiting.

In 106 cases the patient gave a positive reaction to the Mantoux test, but in none was there at any time evidence of active tuberculosis. *Arnold Pines*

945. **The Diagnosis of Bronchogenic Carcinoma in Patients with Pulmonary Tuberculosis**
M. E. SHAFRAN and J. KAVEE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 157–167, Aug., 1955. 4 figs., 14 refs.

At the Montefiore Hospital, New York, during the past 20 years, among 7,847 necropsies performed on male and female patients of all ages with pulmonary tuberculosis 114 cases of primary carcinoma of the lung were found, an over-all incidence of 1·45%. During a recent 12-month period, 73 males over the age of 40 were admitted to the same hospital with pulmonary tuberculosis and in 6 (8·2%) evidence of coexistent carcinoma was found; clinical details of these 6 cases are given. In 4 the diagnosis of bronchogenic carcinoma was suspected before admission because of chest *x*-ray findings, 2 showing a round, homogeneous density with a "fuzzy" circumference, one a typical wedge-shaped shadow arising from the hilum, and one signs of upper-lobe atelectasis with elevation of the horizontal fissure. In the remaining 2 patients the presence of malignant disease was suspected when chemotherapy was started and serial radiographs showed extension and growth of the lesion in one part of the lung and regression of the lesions elsewhere. All 6 patients were heavy smokers and all had a chronic cough; 3 had had haemoptyses, 3 had had chest pain, and 3 were febrile—all these being symptoms which could be attributed to pulmonary tuberculosis.

The most important physical sign differentiating these patients from those with uncomplicated pulmonary tuberculosis was clubbing of the fingers, found in 4 of the 6 cases. In 3 cases bronchoscopy, cytological examination of bronchial washings and sputum, and biopsy of the scalene pad of fat failed to reveal any evidence of carcinoma, and thoracotomy was the only means of confirming the diagnosis. Treatment consisted in lobectomy in one case and radiotherapy in 4 others in

which the lesion was inoperable; one patient died of metastatic carcinoma. In no case was the tuberculosis affected adversely by surgical or irradiation therapy.

The authors describe 7 types of abnormal appearance which, if found in the routine chest radiograph of a patient with tuberculosis, should arouse a suspicion of concomitant bronchogenic carcinoma (although it is realized that they may be very difficult to differentiate from the appearances characteristic of tuberculosis). (1) Infiltration in the anterior segment of the upper lobe. (2) Linear densities resembling vascular shadows, but thicker, somewhat nodular, and failing to taper or branch at the periphery. (3) Faint, amorphous, peripheral infiltrates growing by concentric expansion and with an ill-defined border, increasing in density and becoming more sharply demarcated as the process continues. (4) Dense, round shadows with a " fuzzy " circumference, usually homogeneous, and often accompanied by local obstructive emphysema or hilar lymph-node enlargement. (5) Unilateral enlargement of the hilum. (6) Poorly visualized cavities with a thick, irregular wall. (7) Evidence of erosion and invasion of the first and second ribs, a frequent occurrence with tumours occupying the superior sulcus.

Additional *x*-ray procedures, such as radiography in the oblique and lateral positions and in expiration, tomography, and bronchography, may be helpful. If the presence of a carcinoma is demonstrated the patient must receive chemotherapy for the tuberculous lesion for at least 3 or 4 weeks, at the end of which time, if the carcinoma is considered to be operable and the patient's condition will allow, thoracotomy should be performed, the chemotherapy being continued. *Kenneth Marsh*

946. Survival after Lung Resection for Bronchial Carcinoma

J. R. BIGNALL and A. J. MOON. *Thorax* [*Thorax*] **10**, 183–190, Sept., 1955. 3 figs., 21 refs.

We have studied the duration of life after lung resection for bronchial carcinoma and investigated the effects of various factors on survival in 531 patients treated at the Brompton and London Chest Hospitals between 1940 and 1951. Of these, 453 survived the early post-operative period. Their chance of surviving one year was 63%, 2 years 47%, and 5 years 33%. The 2- and 5-year rates for those reported to have squamous tumours was 52% and 36% compared with 34% and 26% for those with undifferentiated growths. The apparent involvement of the mediastinal nodes at operation had a considerable influence on survival. The 2- and 5-year rates for those without enlarged nodes were 61% and 48%, but for those with enlarged nodes the rates were 27% and 11%.

The prognosis appeared to depend to some extent on the situation of the tumour. The highest survival rates were observed with cancers of the right upper lobe, the 2-year rate being 57%. The left upper and right lower lobes had similar though slightly lower rates. But the 2-year rate with cancers of the left lower lobe was significantly lower, being only 36%. No regular pattern of survival in relation to age was detected.

The prognosis was better in women than in men. The survival rates were lower in those with symptoms for 6 to 8 months than in those with either shorter or longer histories.

The observed differences in survival rates following pneumonectomy and lobectomy could be largely attributed to the smaller proportion with involved mediastinal nodes among those having a lobectomy. The operative mortality decreased from 19% between 1940 and 1946 to 10% in 1950 and 1951. No patient during these 2 years died after a lobectomy, compared with 13% after pneumonectomy. The operative mortality increased with age.—[From the authors' summary.]

947. The Mechanical Properties of the Lungs in Emphysema

J. MEAD, I. LINDGREN, and E. A. GAENSLER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 1005–1016, Part I, July, 1955. 5 figs., 9 refs.

The authors have studied, at Harvard School of Public Health, Boston, the mechanics of breathing in 10 patients with advanced pulmonary emphysema and in 10 normal subjects who acted as controls. Rates of air flow were recorded at the mouth with a pneumotachograph screen and manometer. As a measure of transpulmonary pressures, the difference between the pressure at the mouth and that in the lower third of the oesophagus was recorded by means of an oesophageal balloon on a differential manometer. The use of complicated electronic recording devices enabled the pressure difference between mouth and lung surface to be resolved into its two components, representing the elastic recoil of the lungs and the resistance of the airways respectively.

During quiet breathing, expiration was commonly prolonged among the patients, and pulmonary flow resistance was increased, particularly in expiration. " Pulmonary compliance ", that is, the ratio of volume change to elastic pressure, varied little from that in control subjects. During hyperventilation the resistance of the airway was further increased in expiration. As the rate of breathing increased, pulmonary compliance fell markedly in the patients. During inspiration the atmospheric pressure in the lumen of the airways is greater than the intrapleural pressure outside them; it is this pressure difference which helps to keep the lungs expanded. During forced expiration, however, the pressure difference is reversed and the calibre of the respiratory tract is reduced, thus increasing flow resistance. Clearly, resistance will be increased even more in patients with structural collapse or narrowing of the smaller airways.

The authors discuss the hypothesis above and propound various theories to explain the changes in pulmonary compliance at different rates of breathing. They speculate upon the effect of local changes in the elastic or resistive properties of the lungs and respiratory tract, and point out that those parts with the lowest resistance may become abnormally stressed. Sudden changes in volume, as for example in coughing, accentuate this differential stress and may lead to parenchymal destruction and thus from asthma and bronchitis to emphysema. *D. Goldman*

Urogenital System

948. **Salicylate Therapy of Recurrent Calcium Urolithiasis**

E. L. PRIEN and B. S. WALKER. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 446–451, Sept. 15, 1955. 34 refs.

It has been shown that the urine contains excretory products such as glucuronic acid and its glycosides which form soluble complexes with calcium ions, and that in the presence of infection these solubilizing substances may be partially destroyed or inactivated. One of a large number of compounds known to be excreted in the urine as a glucuronide is salicylate. *In vitro* the presence of crude glucuronide is shown to increase the solubility of calcium and phosphate by 30 to 40%.

The authors, at the Boston University School of Medicine, have treated with 2 g. of aspirin daily for a year or more 19 patients who had suffered from recurring urinary calculi and in all but 3 of whom the urine was infected at the time therapy was started. During this treatment there was no appearance of new calculi and no increase in size or density of existing calculi in 17 of the patients; the treatment failed in 2 cases. The urinary glucuronide output was tripled or quadrupled during aspirin therapy. In 6 other patients who had indwelling urethral catheters and in whom alkaline-encrusting cystitis developed with frequent obstruction of the catheters by stone, aspirin therapy was found entirely to inhibit the encrustation. *E. G. Rees*

949. **Nephrosis Treated by Malaria. Results in 65 Cases**

D. GAIRDNER and P. G. SHUTE. *Lancet* [*Lancet*] **2**, 946–950, Nov. 5, 1955. 2 figs., 13 refs.

In this paper are collated the results in 65 cases of nephrosis which were treated with malaria, 10 by the authors at Addenbrooke's Hospital, Cambridge, information regarding the other 55 being obtained from the physicians concerned. Of the 65 cases, 51 were considered to be cases of "pure" nephrosis, but in 14 there was also azotaemia and hypertension and these were classified as nephritis nephrosis. If a diuresis began any time after the onset of the malarial pyrexia it was ascribed to the malaria, complete remission being defined as loss of all oedema for at least 3 months.

Of the former group, 14 patients (28%) obtained complete remission lasting longer than 3 months and 12 (24%) have remained well during the follow-up period, which has ranged from 5 months to 6 years. No lengthy remissions occurred in the patients with nephritis nephrosis, although partial remission was obtained in 5 cases. It is stated that once a remission was obtained, with complete clearing of the oedema, the most favourable cases showed an early return of the serum albumin and cholesterol levels to normal values; a raised α_2-globulin level and moderate proteinuria did not necessarily indicate impending relapse. In 5 of the cases which responded well to malaria previous hormone therapy had had little or no effect. One death was thought to be due in part to the malaria. Anaemia was the most important complication of treatment, and necessitated blood transfusion in 6 cases. The authors conclude that malaria has a place in the treatment of pure nephrosis, since it induces long-lasting remissions in one-quarter of such patients, and may be effective after hormone treatment has failed. *G. W. Csonka*

950. **Acute Lipoid Nephrosis.** (La néphrose lipoïdique aiguë)

C. HOOFT and C. VANDENBERGHEN. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **185**, 212–224, Oct., 1955. 19 refs.

Between 1939 and 1953 a total of 46 children with lipoid nephrosis were admitted to the Paediatric Clinic of Ghent University, and in the present paper the course of the disease in 20 of these is described. In 10 children, 7 of whom were under 3 years, there was only one episode of oedema, which persisted for 6 to 50 days and then cleared spontaneously. No recurrence was observed during a follow-up period of one year to 15 years, and renal function and blood chemistry remained normal. During the attack the urine contained 2 to 30 g. of protein per litre, and in 4 cases the blood urea level was slightly raised. The clinical and laboratory findings which distinguished the condition from acute nephritis were the normal blood pressure, more severe proteinuria and oedema, greater rise in the plasma cholesterol level (mean 603 mg. per 100 ml.) and in the total plasma globulin and γ-globulin values, and more marked reduction in the plasma albumin concentration. In the remaining 10 children, 8 of whom were over 3 years of age, the clinical and blood chemistry findings were similar during the first 2 months to those observed in the first group, but after that the condition ran a chronic course. No evidence was obtained that treatment influenced the course of lipoid nephrosis.

T. B. Begg

951. **Treatment of Nephrotic Syndrome in Children.** [In English]

P. DURAND and E. DE TONI. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **185**, 225–235, Oct., 1955. 18 refs.

Various forms of treatment of the nephrotic syndrome have been tried at Gaslini Children's Hospital, Genoa, and in this paper the results obtained in 40 children treated since 1949 are analysed. Nitrogen mustard, cation-exchange resin, and thiacetazone were each given to a few patients but the results were unimpressive.

Malaria therapy was found to be of value, infection being induced in 10 patients and 8 to 12 febrile attacks being permitted. In all cases there was an increase in urinary output after 6 or more episodes of fever; in 4 cases the diuresis was not marked, but in the remainder oedema disappeared, proteinuria was reduced, and the plasma protein and serum cholesterol levels returned towards normal. A relapse occurred in one patient

after 4 months, but the other 5 remained well for 10 months to 2 years. In the authors' view malaria should be induced by intramuscular injection of infected blood, there having been an exacerbation of the nephrotic syndrome initially in 3 out of the 5 children infected by mosquito bite.

Repeated courses of large doses of ACTH were also effective. Children under 6 years of age received 100 mg. and those over 6 years 150 to 200 mg. daily for 8 days, this course being repeated after an interval of 3 to 4 days. In all cases antibiotics were given, and if ACTH therapy was prolonged, 1 to 2 g. of potassium chloride daily was added. Initially there was an increase in oedema, but diuresis began towards the end of a course. Oedema disappeared completely in 6 and partially in 3 of the 11 children treated in this way; the results in the remaining 2 were considered to be moderately good. *T. B. Begg*

952. **Biopsy of the Kidney in the Diagnosis and Management of Renal Disease**
R. C. MUEHRCKE, R. M. KARK, and C. L. PIRANI. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 537–546, Sept. 29, 1955. 9 figs., 20 refs.

From the University of Illinois College of Medicine the authors report further experience of their method of percutaneous renal biopsy (Kark and Muehrcke, *Lancet*, 1954, **1**, 1047; *Abstracts of World Medicine*, 1955, **17**, 44) which has been carried out on 179 occasions at three Chicago hospitals, a specimen of renal tissue being obtained in 172 cases. They consider the procedure to be indicated in all types of diffuse renal disease, excluding patients with a bleeding tendency, those with only one kidney, and those with oliguria whose blood non-protein nitrogen level is over 100 mg. per 100 ml. and rising. They do not advise biopsy when there is much calcification of the arteries or when perinephric abscess, hydronephrosis, pyonephrosis, or a renal cyst or neoplasm is suspected.

The patient is admitted to hospital and full preliminary investigations carried out. For the biopsy the patient lies prone with a sandbag under the abdomen. The lower pole of the kidney is first located by means of a fine exploring needle inserted aseptically and under local analgesia between the lowest rib and the lateral border of the quadratus lumborum muscle, the needle describing a characteristic arc on inspiration when its point has penetrated the kidney. In this way the correct depth and direction for the subsequent insertion of the larger Franklin–Vim–Silverman biopsy needle are accurately determined. After the operation the patient remains on the sandbag for 30 minutes to procure haemostasis and is then kept in bed for 24 hours while the blood pressure and pulse rate are recorded frequently. Bleeding into the bladder is most likely to occur during the first half-hour, but each specimen of urine passed in the 24 hours is inspected for the presence of blood. The procedure is usually followed by microscopic haematuria lasting 6 to 12 hours; gross bleeding occurred only in 7 cases and only one patient needed transfusion. The other complications were renal colic due to clot in 3 patients and slight back pain in 5.

Biopsy material is considered adequate if it contains at least 5 glomeruli and adjacent tubules, and examination of such specimens is stated to be of great value for diagnosis and the assessment of response to treatment, as well as for purposes of research in renal cytology and morphology. *L. Capper*

953. **The Clinical Course of Renal Failure Occurring after Intravenous Urography and/or Retrograde Pyelography. Casuistics of 11 Cases (Including 7 Deaths). On Indications for and Risks Involved in the Use of Contrast Media, Including Some Remarks on the Risks of Aspiration Biopsy of the Kidney.** [In English]
N. ALWALL, P. ERLANSON, and A. TORNBERG. *Acta medica Scandinavica* [*Acta med. scand.*] **152**, 163–173, Oct. 12, 1955. 4 figs., 7 refs.

The purpose of this paper is to emphasize the importance of assessing the condition of the kidneys before *x*-ray examination is carried out, so that the risks attendant on the use of opaque medium may be avoided. Between 1952 and 1954, 9 cases of renal failure (7 proving fatal) which occurred after intravenous urography, or intravenous urography followed by retrograde pyelography, were referred to the Renal Clinic, University of Lund, Sweden, these representing most of the severe cases of renal complications after *x*-ray examination seen in Sweden during that time. In addition, the clinic was consulted concerning 2 cases of temporary kidney injury seen at other hospitals. The authors state that in the group of 9 cases an examination with opaque medium "at the stage then existing should not have been necessary"; other diagnostic methods incurring no risk might have proved satisfactory or, at any rate, would have made it clear that the use of opaque medium was either unnecessary or contraindicated.

In each of the 11 cases intravenous urography was undertaken although no test of kidney function had been carried out other than determination of the blood non-protein nitrogen level; in 2 cases urography had been performed when the blood non-protein nitrogen level was raised. Retrograde pyelography (4 cases) was carried out on both sides simultaneously, although it was not necessary to examine both kidneys at the same time. In 3 of the 4 cases the examination was considered necessary because intravenous urography did not reveal any excretion. In 2 cases there was severe pyelovenous backflow bilaterally, yet retrograde pyelography was continued after this complication had already been observed on one side.

The authors admit that the number of cases of renal complications seen (11 in 3 years) is relatively small, having regard to the frequency with which intravenous urography and retrograde pyelography are carried out today. It is difficult in some cases to establish an unequivocal causal connexion between the use of opaque medium and subsequent renal insufficiency, especially in the presence of glomerular nephritis the onset of which may have preceded the radiological examination. It is emphasized that while renal aspiration biopsy carries risks, in selected cases it may be of more diagnostic value than *x*-ray examination. *Adrian V. Adams*

Endocrinology

954. **Male Pseudohermaphroditism: a Hitherto Undescribed Form**
G. I. M. SWYER. *British Medical Journal* [*Brit. med. J.*] 2, 709–712, Sept. 17, 1955. 3 figs., 12 refs.

The author describes, from University College Hospital, London, 2 cases of a new and apparently hitherto unrecognized type of male pseudohermaphroditism. Both patients presented as eunuchoidal females complaining of primary amenorrhoea. In both cases the uterus was rudimentary, the vagina and cervix normal, and mammary development poor; the urinary 17-ketosteroid excretion was normal. The chromosomal (genetic) sex, as determined by blood-film studies (the polymorphonuclear leucocyte test) and confirmed by skin biopsy examination, was male. Both patients were treated with female sex hormones, one with stilboestrol and the other with ethinyloestradiol, and scanty oestrogen-withdrawal bleedings were noted. In both a little mammary enlargement occurred in the course of 3 months.
G. B. West

THYROID GLAND

955. **Pitfalls in Diagnostic Use of Radioactive Iodine**
S. SILVER, S. B. YOHALEM, and R. A. NEWBURGER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1–5, Sept. 3, 1955. 18 refs.

The authors, working at the Mount Sinai Hospital, New York, attempt to show that the use of tracer doses of radioactive iodine (^{131}I) in the diagnosis of thyroid disease has its limitations. The investigation was carried out on 113 patients who, in the opinion of at least two experienced clinicians, were undoubtedly euthyroid; in many instances the clinical diagnosis was confirmed by the results of estimation of the basal metabolic rate and of the serum protein-bound ^{131}I level. In all cases the uptake of ^{131}I by the thyroid gland was determined 24 hours after oral administration of 25 to 100 μc. of carrier-free ^{131}I, values up to 55% being considered normal, and the concentration of protein-bound ^{131}I in the plasma was estimated 72 hours after administration of the same tracer dose.

In 33 of the 113 patients the uptake of ^{131}I by the thyroid gland was high (above 55%), but the serum protein-bound ^{131}I level was normal; only 2 of these patients had had hyperthyroidism. In 51 patients, 46 of whom had been "cured" of hyperthyroidism, the uptake of ^{131}I was normal, but the protein-bound ^{131}I level was raised. In the remaining 29 patients the uptake of ^{131}I by the thyroid gland was high and the serum protein-bound ^{131}I level was increased; 27 of these patients had been "cured" of hyperthyroidism.

The authors discuss possible reasons for the increased ^{131}I uptake in euthyroid subjects, and suggest that the mechanisms involved may be related to a decrease in the iodide concentration in the total body water and a diminished hormonal iodine pool in the thyroid gland. They consider that in view of these "false hyperthyroid" reactions, the results of ^{131}I tests should be interpreted with due regard to the clinical condition of the patient.
D. G. Adamson

956. **Studies on Radioiodine Treatment of Thyrotoxicosis. With Special Reference to the Behaviour of the Radioiodine Tracer Tests.** [In English]
L. LARSSON. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] Suppl. 126, 1–164, 1955. 63 figs., bibliography.

957. **Radioactive Iodine or Surgery in Treatment of Hyperthyroidism**
D. E. CLARK and J. H. RULE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 995–997, Nov. 5, 1955. 1 fig., 4 refs.

958. **Hypothermic Coma in Myxoedema**
M. MALDEN. *British Medical Journal* [*Brit. med. J.*] 2, 764–766, Sept. 24, 1955. 11 refs.

The author describes, from Ancoats Hospital, Manchester, 3 cases of hypothermic coma in myxoedematous patients, all women in the early sixties, in whom rectal temperatures as low as 78° F. (25·5° C.) were recorded. Two of the patients died, and post-mortem examination revealed Riedel's thyroiditis in one case and Hashimoto's disease in the other, but the adrenal and pituitary glands were normal. The third patient recovered following treatment with intravenous thyroxine and ACTH (corticotrophin), despite the fact that she was comatose for 2 days and semi-comatose for the next 10 days. The characteristic cadaver-like dry coldness of the skin of these patients is vividly described.

Because of the lack of sufficient information it was not possible to ascertain the cause of the hypothermia, but an analysis of the available findings in these 3 and in 6 other similar cases reported in the literature showed that subnormal temperatures were recorded in all 9 patients. The blood sugar level was normal, but in 4 of the published cases the serum sodium and chloride levels were low and in 2 of them the serum potassium level was high, these changes being similar to those found in adrenocortical failure or hypopituitarism. In one of the author's patients the serum sodium, chloride, and potassium concentrations were all low, but that of the blood urea was normal. These findings, which are suggestive of water retention, preceded the onset of coma.

The absence of shivering despite the low body temperature and the ease with which the latter could be raised by the application of heat suggested that there was failure of the thermoregulatory centre.
D. G. Adamson

959. **Myxoedema Coma in a Patient with Hashimoto's Struma**

L. KARHAUSEN and S. ZYLBERSZAC. *British Medical Journal* [*Brit. med. J.*] **2**, 766–768, Sept. 24, 1955. 1 fig., 3 refs.

The authors present, from the Centre Anticancéreux, University of Brussels, a detailed account of the clinical features, biochemical data, and post-mortem findings in a myxoedematous female patient aged 63 who died in coma. On admission the patient had the clinical features of gross myxoedema with a basal metabolic rate of −8%, and studies with radioactive iodine showed no significant concentration in the thyroid gland. She was apathetic but fully conscious. From the 9th day onward her condition deteriorated and by the 13th day there was marked hypotension and a myasthenic state which did not respond to neostigmine. The serum electrolyte level was normal and that of the blood urea was 61 mg. per 100 ml. The temperature rose to 100·4° F. (38° C.). Treatment with 1 mg. of thyroxine intravenously and 100 mg. of cortisone by mouth produced no improvement and the patient died on the 16th day after admission.

Post-mortem examination showed an atrophic thyroid gland weighing 9 g. with lymphoid infiltration, the appearance being that of Hashimoto's struma. The adrenal glands were normal; the anterior lobe of the pituitary gland showed numerous acidophilic cells but no increase in basophil cells. The only abnormality found in the central nervous system was that the supraoptic nuclei contained numerous cells with an eccentric nucleus and large Nissl bodies at the periphery. Although there was marked atheroma of the aorta and coronary arteries, no coronary occlusion was found.

The authors point out that hypothermia, often described in patients with myxoedema coma, did not occur in this case, and cannot therefore be implicated as a general explanation for the death of myxoedematous patients. They suggest that consideration should be given to a possible neural factor, in view of the abnormal histological appearances of the supraoptic nuclei observed in this case. *D. G. Adamson*

ADRENAL GLANDS

960. **Metabolic Changes and Therapeutic Considerations in Bilateral Adrenalectomy**

I. G. GRABER and P. BEACONSFIELD. *British Medical Journal* [*Brit. med. J.*] **2**, 704–708, Sept. 17, 1955. 4 figs., 23 refs.

At Hammersmith Hospital (Postgraduate Medical School of London) the metabolic changes were observed in 3 patients with carcinoma of the breast and widespread metastases who were subjected to bilateral adrenalectomy. On the day before the operation varying doses of deoxycortone acetate, cortisone (both by mouth and intramuscularly), and sodium chloride were given, and complete routine clinical laboratory estimations carried out. For the first 5 days after operation a period of relative sodium retention was generally noted, followed by a period of early sodium diuresis lasting another 5 or 6 days. A short period of relative sodium retention was followed by an indefinite period of late sodium diuresis. This latter period was characterized by an increase in the percentage excretion of water, sodium, and potassium equal to, or greater than, the preoperative values, with maintenance of the high glomerular filtration rate. This phase of permanent sodium diuresis in adrenalectomized patients is not unlike that of patients with Addison's disease adequately treated with cortisone.

G. B. West

961. **Cushing's Disease. The Surgical Experience in the Care of 46 Cases**

O. COPE and J. W. RAKER. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 119–127 and 165–172, July 28 and Aug. 4, 1955. 7 figs., bibliography.

The authors point out that although Cushing considered the syndrome which bears his name to be a pluriglandular one in which a basophilic adenoma of the anterior lobe of the pituitary gland played a dominant role, subsequent experience has cast doubt on this concept. Thus cases have occurred in which no pituitary adenoma could be found at necropsy and in which adrenocortical tumours were present, while treatment—with *x* rays and testosterone—directed at the pituitary is often ineffective and resection of the adrenal glands has proved to be the most reliable form of therapy. These observations suggest that the adrenal cortex is primarily at fault, and this is supported by the fact that all the manifestations of Cushing's syndrome may be produced during ACTH and cortisone therapy.

Of 46 patients with Cushing's syndrome treated at the Massachusetts General Hospital, Boston, since 1935, 36 were female and 10 male, the average age being 35 years. The symptomatology of the condition, as exemplified by these cases, varies with the relative prominence of the effects of the various adrenocortical hormones, fatigue, weakness, weight gain, obesity, and changed appearance being the most common complaints. Of the many physical signs, the "moon face" and obesity of the trunk with wasting of the limbs are the most striking. Atrophy of the corium results in striae in the skin over the fat-laden areas, with florid facies and blotchy extremities; acne, pigmentation, and trophic ulcers also occur, and in women hirsutism is frequent. Muscular wasting is the most constant sign, and vascular hypertension is often present (in half of the present series). Osteoporosis is common, and is the cause of skeletal and occasionally of root pain. Evidence of gonadal suppression is often found, and diabetes mellitus may occur (5 cases). In 13 of the authors' cases there was psychological disturbance.

The chief pathological changes occur in the supporting tissues of mesenchymal origin and in the endocrine glands. In the former atrophy is outstanding; the excess of fat found in the subcutaneous tissues of the trunk may be associated with fatty infiltration of muscles. A loss of resilience and strength is also found in the blood vessels and may account for the frequent bruising and the spontaneous haemorrhages which sometimes occur; arteriosclerosis may develop later. Atrophy of the bone matrix with decalcification may cause spon-

taneous fractures in fully developed cases. In none of the authors' cases was sellar enlargement demonstrable radiologically and in none of the 7 coming to necropsy was a basophil pituitary adenoma found, whereas in every case the adrenal cortex was enlarged either by neoplasia or hyperplasia. Where the condition of the ovaries was investigated at operation gross atrophy was found. No case of thymic tumour was encountered. The laboratory findings in respect of urinary steroid excretion and electrolyte metabolism are reported and briefly discussed.

Non-surgical treatment offers relatively little, although *x*-irradiation of the pituitary fossa may produce a temporary remission while testosterone increases general well-being. Surgical treatment is limited to removal of an adrenocortical tumour if present, but in the absence of a tumour bilateral subtotal adrenalectomy is necessary to achieve the required reduction of secretory activity. The preoperative detection of a tumour is thus of importance if unnecessary bilateral exposure of the glands is to be avoided. While such a diagnosis may be indicated by a palpable tumour, by pain in cases of carcinoma, or by a short history, radiography is the most efficient method. For this purpose the authors consider that good plain films of the abdomen taken after adequate preparation will give as much information as those following peri-adrenal air insufflation. [For details of the authors' surgical technique and pre- and post-operative treatment the original paper should be consulted.]

Of the 46 patients treated, 5 had malignant adrenocortical tumours and all died, only 2 having had surgical treatment. Of 12 patients with cortical adenoma, one died without operation and 11 were treated surgically, one dying and the remaining 10 being relieved of their disease. Of the 27 patients with cortical hyperplasia, 2 died without surgery and 2 died following inadequate adrenalectomy; 23 were subjected to subtotal adrenalectomy and 19 of these were relieved of their disease, 2 others being unrelieved by operation, while one died of pulmonary embolism and one of renal sepsis after operation.

[This excellent record of 20 years' experience of Cushing's syndrome is a most valuable contribution to a subject concerning which there has been much confusion.] *J. E. A. O'Connell*

962. **On the Secretion of Noradrenaline following Reflex Excitation of the Adrenal Glands.** (О выделении норадреналина при рефлекторном возбуждении надпочечника)

A. N. Poskalenko. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **1**, 92–96, No. 5, Sept.–Oct., 1955. 2 figs., 9 refs.

The reflex secretion of adrenomedullary hormones was studied in decerebrated cats at the Institute of Sanitation and Hygiene, Leningrad. Chemoreceptors of the carotid body (in a series of 6 experiments) and the isolated carotid sinus (in another series of 11 experiments) were acted upon by solutions of potassium cyanide ranging in strength from 1 in 5,000 to 1 in 10,000. The ensuing changes in blood pressure, contraction of the nictitating membrane, and the degree and distribution of vasoconstriction were compared with the effects produced by adrenaline. All the reactions tended to show that reflex stimulation of the adrenal medulla from the carotid body and carotid sinus led to the secretion of noradrenaline-like substances in addition to adrenaline itself.

A. Swan

963. **Aldosterone: Observations on the Regulation of Sodium and Potassium Balance**

J. A. Luetscher and R. H. Curtis. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 658–666, Oct., 1955. 4 figs., 21 refs.

See also Pharmacology, Abstract 861.

DIABETES MELLITUS

964. **A Concept of Diabetes**

W. P. U. Jackson. *Lancet* [*Lancet*] **2**, 625–631, Sept. 24, 1955. 19 figs., bibliography.

The author suggests that diabetes mellitus is an innate obscure disorder of carbohydrate metabolism which has been present long before hyperglycaemia develops —in fact from birth. In the latent or "prediabetic" stage there may be abnormalities of carbohydrate tolerance which are not gross enough to be accepted (at present) as evidence of diabetes or which occur only during temporary states of stress. There may be disturbances of growth and of the vascular structure of affected subjects, and their offspring may show unusual features.

The evidence offered in support of this hypothesis includes: the abnormal obstetric patterns, similar to those of frankly diabetic mothers, shown by women years or even decades before they develop overt diabetes; the tendency for prediabetic as well as diabetic men to father a higher proportion of overweight babies than do normal men; and the not infrequent occurrence of demonstrably diminished carbohydrate tolerance during pregnancy in women who later develop diabetes. Published work on these subjects by the author and others is reviewed and some additional clinical observations are provided. The "temporary" diabetes which may occur during pregnancy, staphylococcal infections, endocrine states such as Cushing's syndrome and hyperthyroidism, and during treatment with corticotrophin (ACTH) or glucocorticoids is cited as evidence that in "normal" persons an underlying diabetic tendency may be present which can be made manifest by further impairment of carbohydrate tolerance, such diabetic episodes being apparently more likely to occur in those with a family history of the disease.

The parts played by growth hormone and by glucocorticoids in the production of the foetal abnormalities associated with diabetes and in the pathogenesis of diabetes itself are discussed. The author points out that the newborn infants of diabetic mothers often show hyperplasia of the islets of Langerhans similar to that

induced in animals by diabetogenic substances such as growth hormone, and that abnormal glucose tolerance curves are found more frequently in the children of diabetic mothers than in those of diabetic fathers. He deduces that familial diabetes is not entirely hereditary in origin, but is partly also congenital when the mother is diabetic, owing to the diabetogenic effect on the foetus of the diabetic maternal environment. He concludes that since many features of the diabetic state are present before glycosuria and hyperglycaemia make it evident, and may even be present at birth, the term diabetes should not be restricted to the hyperglycaemic phase alone. *H.-J. B. Galbraith*

965. **Peripheral Vascular Disorders in Diabetes Mellitus. A Survey of 3000 Cases**
D. W. KRAMER and P. K. PERILSTEIN. *Angiology* [*Angiology*] **6**, 408–416, Oct., 1955. 23 refs.

The incidence of peripheral vascular disorders in diabetes mellitus was studied from the records of 3,000 diabetic patients admitted consecutively to the Jefferson Medical College, Philadelphia. The first 1,000 cases were seen between 1920 and 1930, the second between 1931 and 1941, and the third between 1942 and 1951. The incidence of peripheral vascular complications, whether potential, threatened, or obvious gangrene, was 17·3% in the first 1,000 cases, 21·6% in the second, and 50·7% in the third. In a further analysis of the last 1,000 cases no clear relationship was found between the frequency of vascular complications and the duration or severity of the diabetes (as assessed by insulin dosage), but there was a tendency for the incidence to increase with age.

[The authors' finding that the incidence of these complications was unrelated to the duration of the diabetes is contrary to that of some British workers, not cited in the list of references.] *P. Hugh-Jones*

966. **Glucagon as a Regulator of Insulin Function**
G. E. ANDERSON. *Science* [*Science*] **122**, 457–459, Sept. 9, 1955. 4 figs., 9 refs.

The author, writing from the State University of New York College of Medicine, New York, presents evidence which suggests that in normal individuals insulin and glucagon are not antagonistic, as has been previously stated, but mutually synergistic. Experiments in animals and man resulted in the following observations. (1) Glucagon acts as a potentiator of insulin function, further raising or further lowering the blood glucose level in the post-absorptive stage, depending on which phase of the blood glucose curve is being exposed to the hormone when the glucagon is injected. (2) Glucagon seems to serve as a trigger mechanism to insulin function throughout the post-absorptive period, much as glucose acts as the inciter of insulin function during the absorptive state. (3) In individuals with low mean fasting blood glucose levels a small dose (1 to 3 units) of glucagon-free insulin given intravenously caused initially a prompt rise rather than a fall in the blood glucose level; it is considered likely that this resulted from the action of intrinsic glucagon "triggered off" by the insulin. (4) There is some evidence that under certain circumstances glucagon may be capable of acting through enzyme systems other than hepatic phosphorylase in the release of glucose from glycogen. The many and probably important implications of these observations in clinical diabetes are briefly mentioned, but not discussed. *A. I. Suchett-Kaye*

967. **Insulin Lipodystrophy. A Clinical and Experimental Study.** (Les lipodystrophies insuliniques. Étude clinique et expérimentale)
H. CHIMÈNES. *Diabète* [*Diabète*] **3**, 105–122, July–Aug., 1955. Bibliography.

The author reports a clinical and experimental study of the lipodystrophy which occasionally develops at the site of insulin injections in diabetic patients. He found the incidence to be 1 to 2%, and presents his findings in 18 cases of the condition. The lipodystrophy usually appeared within 5 years of the start of insulin injections, and was found only in children and in women of childbearing age. Among the various changes seen at the site of insulin injection were hypertrophy (9 cases), atrophy (17), or both (8); the condition was apparently not related to any particular type of insulin. It is not known if the size of the dose of insulin is an important factor in causing the condition; the doses in the present series ranged from 20 to 124 units per day, average 71 units, but the author points out that these high doses may have been due to attempts to compensate for the insulin lost by injection into the lipodystrophic areas. Biopsy examination in 4 cases showed atrophy of the subcutaneous tissues in all of them and sclerotic changes attributed to foreign-body reactions to the injected insulin in 3.

In experiments on normal and alloxan-diabetic rats the effects of sex, castration, pregnancy, and oestrogen and androgen therapy on the local reaction to insulin were investigated by measuring the wet and dry weights and insulin indices of subcutaneous fat from the sites of injection. Lipodystrophy occurred in normal as well as in diabetic animals, both male and female, but the tendency to do so was apparently diminished by the administration of testosterone propionate.

Therapeutic measures were tried in 13 patients, in whom the insulin injections were made in rotation into 60 sites on the abdomen, thighs, and shoulders at points over 1 cm. apart, 40 to 100 mg. of testosterone propionate being injected at weekly intervals at remote sites. In all cases the control of the diabetes was improved and in 11 the insulin dosage could be reduced. The exact mode of action of androgen in hastening the disappearance of insulin lipodystrophy is not clear.
W. J. H. Butterfield

968. **The Employment of Certain Sulphonamides in the Treatment of Experimental Diabetes Mellitus. Personal Researches (1942–6).** (L'utilisation de certaines substances sulfamidées dans le traitement du diabète sucré expérimental. Recherches personnelles (1942–1946))
A. LOUBATIÈRES. *Presse Médicale* [*Presse méd.*] **63**, 1701–1703, Dec. 10, 1955.

The Rheumatic Diseases

969. **Corticotrophin and Cortisone in the Treatment of Scleroderma**
M. M. ZION, B. GOLDBERG, and M. M. SUZMAN. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 215–227, July, 1955. 2 figs., 11 refs.

Cortisone and corticotrophin were given at Johannesburg General Hospital, South Africa, to 14 patients (7 females and 7 males) suffering from scleroderma. Striking improvement was obtained in 4 patients and slight improvement in 9; in one patient no subjective or objective change was observed. In one case there was clinical and histological reversal to normal. The duration of the disease appeared to influence the results since none of the patients with symptoms of more than six months' duration derived much benefit. The best results were obtained in patients without any peripheral vascular disturbance; 9 of the 10 patients in whom there was little or no response suffered from Raynaud's disease. Improvement was not maintained when treatment was temporarily discontinued. No difference was observed between the response to cortisone and that to corticotrophin. *E. W. Prosser Thomas*

970. **Metacortandracin and 9-*alpha*-Fluorohydrocortisone Acetate in Rheumatic Diseases**
L. VILLA, C. B. BALLABIO, and G. SALA. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 251–258, Sept., 1955. 3 figs., 25 refs.

"Metacortandracin" (prednisone) and 9-α-fluorohydrocortisone, recently introduced as steroids with increased anti-inflammatory action and negligible effect on electrolyte balance and nitrogen metabolism as compared with cortisone, were the subject of clinical trials on 36 patients with a variety of acute and chronic rheumatic diseases at the Medical Clinic of the University of Milan. Both steroids were given by mouth, the initial dose of the former being 30 to 50 mg. and of the latter 8 to 16 mg. Marked subjective and objective improvement took place within a few days, that in articular function in cases of rheumatoid arthritis being greater in many cases than had previously been obtained with cortisone; the erythrocyte sedimentation rate, too, seemed to decrease more rapidly. Prednisone was found to have an anti-rheumatic effect 3 to 5 times greater than that of cortisone, while that of 9-α-fluorohydrocortisone was 8 to 10 times greater. The latter drug, however, caused marked electrolyte imbalance, whereas the former affected this so little that it could safely be used in cases of active carditis with heart failure. Both drugs caused hirsutism, rounding of the face, and other side-effects attributable to increased corticoid activity.

The fact that 9-α-fluorohydrocortisone has a powerful mineralocorticoid action suggests that there is no close association between the metabolic and anti-inflammatory properties of the corticoids. *David Preiskel*

971. **Potentiation of the Antirheumatic Efficacy of Sodium Salicylate by Intravenous Administration in Hypertonic Glucose Solution.** (Potenziamento dell'efficacia antireumatica del salicilato di sodio mediante somministrazione endovenosa in soluzione glucosata ipertonica)
L. PEROSA and P. DE VITA. *Riforma medica* [*Rif. med.*] **69**, 1125–1131, Oct. 8, 1955. 17 figs.

At the University Institute of Clinical Medicine, Bari, the authors have treated 15 patients with rheumatic fever with intravenous drip infusions of 6 to 8 g. of sodium salicylate dissolved in a litre of 40% hypertonic glucose solution and given over a period of 6 to 8 hours. They claim results superior to those achieved with any other form of salicylate medication. *L. Michaelis*

972. **Erythema Marginatum**
J. B. BURKE. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 359–365, Aug., 1955. 5 figs.

The literature on erythema marginatum is reviewed and 19 cases seen at the Children's Hospital, Sheffield, and the Hospital for Sick Children, Great Ormond Street, London, are described. Of the 19 children, aged 7 weeks to 13 years, 14 had rheumatic fever and one had nephritis. The duration of the rash varied from a few days to 2½ months, and tended to recur. Administration of salicylates, cortisone, or ACTH did not influence the course of the condition and the appearance of the rash did not seem to be an indication of rheumatic activity.

It is considered that although erythema marginatum and rheumatic fever are commonly associated, the former must be considered to be a non-specific phenomenon since it occurs in the absence of rheumatic fever.

Kathleen M. Lawther

See Pathology, Abstract 822.

CHRONIC RHEUMATISM

973. **Chronic Arthritis after Recurrent Rheumatic Fever**
A. E. THOMAS. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 259–266, Sept., 1955. 4 figs., 30 refs.

Although it is known that between 20 and 50% of patients with rheumatic fever eventually develop chronic heart disease, the polyarthritis which accompanies the acute carditis is generally regarded as completely reversible. However, the development of chronic arthritis after an attack of rheumatic fever was described by Jaccoud in 1869, and more recently an incidence of chronic arthritis following acute rheumatism in 20 to 30% of cases has been reported by Scandinavian workers. While these figures are probably too high, there are a number of reports in the literature of an abnormal incidence of cardiac valvular lesions in cases of chronic arthritis, particularly spondylitis.

Of the 55 patients attending the Rheumatism Clinic at the Manchester Royal Infirmary between 1948 and 1953 who were recorded as having valvular disease of the heart, 29 were reexamined. Evidence of rheumatoid arthritis was sought in the form of a symmetrical polyarthritis affecting the small joints of the hands and feet, supporting evidence being provided by vasospasm, excessive sweating of the extremities, lymphadenopathy, and necrobiotic nodules.

In 14 of the cases most of these manifestations were present, with confirmatory radiological findings in the majority. All but one of these patients had mitral valvular disease. In 11 of the remaining cases the patient complained of recurrent attacks of febrile polyarthritis, usually preceded by upper respiratory infection and responding to the administration of aspirin, which were diagnosed as recurrent attacks of rheumatic fever; their heart disease was more severe and progressive than that of the former group. A relatively high incidence of spinal involvement, with limitation of movement and, in 2 cases, ankylosis of the whole spine, in the second group may be explained by the fact that a number of the patients were drawn from a clinic for the diagnosis of ankylosing spondylitis. On the other hand there were certain differences from the typical picture of ankylosing spondylitis—for example, the history of repeated attacks of rheumatic fever, the presence of tendon nodules, and unusual radiographic changes in the sacro-iliac joints. Moreover, 10 of these 11 patients showed changes in the peripheral joints which in 4 cases resembled those described by Jaccoud.

If it be accepted that these patients were suffering from recurrent rheumatic fever, then their joint lesions may have been caused by this process. Alternatively, some of them were possibly suffering from a recurrent acute febrile form of ankylosing spondylitis with cardiac involvement or simply from recurrent rheumatic fever with a coincident ankylosing spondylitis. The bacteriological and serological study of this type of case during the acute episodes may throw fresh light on the problem of its nature. *David Preiskel*

974. **Effect of Cortisone and Certain Other Steroids on the Peripheral Vasculature in Arthritis**
A. Woodmansey and J. W. Beattie. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 293–297, Sept., 1955. 7 figs., 20 refs.

The effect of cortisone and of 4 other steroids (deoxycortone acetate, testosterone, progesterone, and oestradiol) on the peripheral vasculature of patients with rheumatoid arthritis and osteoarthritis was studied at the General Infirmary at Leeds. A persistent improvement in the results of the thermal-response test was noted only after administration of cortisone. Moreover, the rheumatic condition improved in patients given cortisone but was uninfluenced in those given the other steroids.

The authors claim that these findings lend further support to their view that the action of cortisone is neurovascular, through the thermoregulatory mechanism. *J. Warwick Butler*

975. **Autoantibodies in Rheumatoid Arthritis.** (Autoanticuerpos en la poliartritis crónica progresiva)
A. Foz and E. Batalla. *Revista española de reumatismo y enfermedades osteoarticulares* [*Rev. esp. Reum.*] 6, 142–153, July, 1955.

Working at the Municipal Hospital for Infectious Diseases, Barcelona, the authors have devised a test for rheumatoid arthritis which gave a positive result in 24 out of 32 patients with the disease, and a negative result in 140 out of 144 control subjects. In this test, which is claimed to be more specific and more sensitive than the Waaler–Rose test, the serum to be tested is added in varying dilutions to a suspension of *Brucella* which has been "sensitized" by incubation for one hour at 37° C. with serum from a patient with brucellosis. The serum chosen for this purpose is one poor in complete (agglutinating) antibodies and rich in incomplete antibodies against *Brucella*, the globulins containing these antibodies being adsorbed by the organisms in the suspension. The addition of serum from a case of rheumatoid arthritis then causes agglutination of the brucellae owing to its content of antibodies to human globulin. Control tests are carried out with non-sensitized suspensions. *L. Michaelis*

976. **Diphenylamine Reaction in Rheumatoid Arthritis**
G. R. Fearnley, J. Pirkis, N. de Coek, R. Lackner, and R. I. Meanock. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 226–231, Sept., 1955. 7 figs., 3 refs.

From time to time new tests of activity in rheumatoid arthritis are described, one of these being the colour intensity obtained when a protein-free precipitate of plasma or serum is treated with Dische's diphenylamine reagent under defined conditions. Since, however, a new test is acceptable only if it proves to be superior to determination of the erythrocyte sedimentation rate (E.S.R.), which is easy and simple to carry out, an investigation was undertaken at the Postgraduate Medical School of London in 55 patients (aged 20 to 70 years), 23 of whom had rheumatoid arthritis and 32 had no evidence of the disease, to determine: (1) the correlation, if any, between the blood response to diphenylamine and the E.S.R.; (2) the response to diphenylamine in patients given steroid therapy; and (3) the value of the response as a measure of activity in the small number of patients with clinically active rheumatoid arthritis and a normal E.S.R.

The E.S.R. was increased (above 15 mm. at one hour Westergren) in 27 out of 34 determinations on patients with clinically active rheumatoid arthritis, and in 25 of the 27 the diphenylamine reaction was above normal. Of the 7 instances in which the E.S.R. was normal there was an increased diphenylamine reaction in only 2. In patients receiving steroid therapy the response to diphenylamine was below normal, but in some patients there were unexpected fluctuations not reflected by the E.S.R.

The authors conclude that the reaction of the serum to diphenylamine is not more sensitive than the E.S.R. as an indication of rheumatic activity, and they empha-

size that before a test of such activity can be recommended as a routine procedure it must be shown to possess some practical advantage over other, well-established tests. *P. I. Reed*

977. **Serum Diphenylamine Reaction in Rheumatoid Arthritis**

E. Cecchi and F. Ferraris. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 267–270, Sept., 1955. 2 figs., 5 refs.

At the Rheumatic Centre, Rome, the variations in the colour reaction of the blood to diphenylamine were studied in 30 patients with rheumatoid arthritis and 30 who were free from acute disease, the findings being compared with the erythrocyte sedimentation rate (E.S.R.). The reaction was observed for a period of 33 days, during which time phenylbutazone, or hydrocortisone, or a combination of the two drugs was given by mouth.

In 8 patients with chronic rheumatoid arthritis the diphenylamine response and the E.S.R. were within normal limits throughout the period of observation. In 22 patients in the active stage of the disease both the colorimetric value for the diphenylamine reaction and the E.S.R. were consistently high at the start, but by the 30th day the diphenylamine response was normal in 18 of them, although the E.S.R. was normal in only 12. The fall in the diphenylamine value paralleled an improvement in the clinical state, and was most marked in patients given hydrocortisone alone or in combination with phenylbutazone. No significant variation from normal values was observed either in cases of rheumatoid arthritis of long duration or in cases of ankylosing spondylitis.

The authors conclude that as a measure of disease activity and of the efficacy of the treatment the diphenylamine reaction is, in general, more sensitive than the E.S.R. *P. I. Reed*

978. **Oral Hydrocortisone Therapy in Rheumatoid Arthritis. An Appraisal of General Results of Prolonged Administration**

E. W. Boland. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 232–237, Sept., 1955. 5 figs., 20 refs.

Preliminary clinical observations on hydrocortisone in 1951 suggested that its anti-inflammatory action was much the same as that of cortisone, but was accompanied by fewer side-effects. Since then the author has used the drug in the treatment of 150 cases of rheumatoid arthritis for periods of 9 to 36 months. All the patients treated had previously failed to respond to conservative treatment; mild cases were excluded. The initial suppressive dose of hydrocortisone was 50 to 70 mg. daily in the most severe cases, and this was diminished by 5 mg. every 7 to 14 days until the smallest dose was reached which would control the manifestations adequately; in severe cases this was 45 to 65 mg. daily. Minor endocrine side-effects were disregarded, and in only 2 cases had treatment to be stopped because of complications attributable to the drug, but in 37 cases side-reactions prevented the use of the most effective dose. Improvement was regarded as satisfactory in 59% of cases, a remission of symptoms being more common in those of moderate severity than in those in which the disease was more severe. Moreover, the results were better with arthritis of recent origin, the critical point beyond which the response began to fall off being about 2 years after the onset. In 50 cases there was evidence of progression of the disease during treatment, but in 19 of these the patient's functional capacity did not appear to have diminished significantly (as it had in the remaining 31 cases).

It is concluded that hydrocortisone, although a valuable drug, is far from being an ideal suppressive agent against rheumatoid arthritis, and the hope is expressed that new steroids will eventually be found possessing greater anti-inflammatory powers and less unwanted physiological activity than do those available at present. *David Preiskel*

979. **The Results of Prolonged Adrenocortical Therapy in 38 Cases of Rheumatoid Arthritis.** (Résultats de la corticothérapie prolongée dans 38 cas de rhumatismes inflammatoires chroniques)

J. Arlet, A. Rascol, and J. Mole. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 595–604, July–Aug., 1955. 1 fig., 7 refs.

The authors describe their methods of assessment and results [similar to those reported from the U.S.A. and Great Britain] in the treatment of 38 cases of rheumatoid arthritis. Only 2 cases did not respond to treatment with cortisone by mouth over periods from 3 to 28 months; a final maintenance dose of 25 to 87·5 mg. a day was found to be required. In no case did complications necessitate discontinuance of treatment. Gold therapy was given in addition in 17 cases, but it did not make any very obvious difference to the outcome. A few severe cases appear to need 75 mg. of cortisone per day indefinitely; with cheaper methods of manufacture of the hormone now under way this dosage seems to be feasible. *G. S. Crockett*

980. **Long-term Treatment with Cortisone.** (Traitement à long terme par la cortisone)

J. Toussaint. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 605–610, July–Aug., 1955.

The author describes his experience at the Hospital for Special Surgery, New York, in the treatment of 27 cases of rheumatoid arthritis and 5 of ankylosing spondylitis with cortisone or hydrocortisone for periods of 6 to 42 months. The effect of treatment was assessed by using Steinbrocker's method of classification. The final maintenance dose was found to be between 50 and 75 mg. per day by mouth. In about half the cases there was partial or complete cessation of activity of the disease process, even after treatment was discontinued. The long-term treatment of rheumatoid arthritis with small oral doses of cortisone seems to be gaining favour. In only one patient, in whom a peptic ulcer developed, did side-effects necessitate cessation of the treatment. *G. S. Crockett*

Physical Medicine

981. **The Effect of Breathing Exercises in Pulmonary Emphysema**
J. D. SINCLAIR. *Thorax* [*Thorax*] **10**, 246–249, Sept., 1955. 10 refs.

In a group of 31 patients with clinical, radiographic, and physiological signs of emphysema the response to the usual breathing exercises was assessed at Green Lane Hospital, Auckland, by standard tests of pulmonary function. A slight improvement in the average results for each of the tests was found after a course of exercises, which was not statistically significant and was due chiefly to marked improvement in a few cases. There was no correlation between the degree of subjective improvement and the results of any of the standard tests. An apparent increase in diaphragmatic excursion, noted in nearly all the patients, was shown to be due to reduction of elevation of the chest wall during inspiration. This was the one constant achievement of physiotherapy, and it is suggested once again that the relief of dyspnoea in some emphysematous patients is due to elimination of wasteful inspiratory effort. *P. Mestitz*

982. **An Assessment of the Value of Breathing Exercises in Chronic Bronchitis and Asthma**
R. S. MCNEILL and J. M. MCKENZIE. *Thorax* [*Thorax*] **10**, 250–252, Sept., 1955. 12 refs.

At Maryfield Hospital, Dundee, 17 patients with recurrent asthma or bronchitis were given instruction in the breathing exercises recommended by the Asthma Research Council; 8 others were given a course of ultraviolet irradiation. The expiratory flow rate (Kennedy, *Thorax*, 1953, **8**, 73) was measured before and after treatment in both groups. There was an average improvement of 4% in the first group, and a deterioration of 2% in the second group; neither of these figures is statistically significant. The results, though not conclusive, throw further doubt on the value of breathing exercises in asthma and bronchitis. *P. Mestitz*

983. **Effect of Various Exercise Programs on Isometric Tension, Endurance and Reaction Time in the Human**
A. D. BAER, J. W. GERSTEN, B. M. ROBERTSON, and H. DINKEN. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 495–502, Aug., 1955. 7 figs., 24 refs.

The effect of various exercise programmes on the isometric tension, endurance, and reaction time of the flexors of the wrist was studied in 63 normal subjects at the University of Colorado School of Medicine, Denver, by means of a strain-gauge dynamometer. Resisted exercises, both isotonic and isometric, were performed by different groups at various contraction rates from 10 to 30 a minute, and the effects compared with those of low-resistance exercises. Resisted exercises had a more rapid effect than unresisted, but after 6 weeks no real difference in effect could be detected between the various regimens, isotonic resisted exercises coming out slightly the best. Reaction time was increased after a course of resisted exercises, but this finding was considered to be of doubtful significance. Isometric tension was regularly increased to a considerable degree, especially by exercises at the slower contraction rates. Endurance was increased by all regimens. The most interesting finding was that a marked increase in work capacity, ranging from 115 to 133%, was produced by all the exercises tested, whether of high-resistance or low-resistance type. *R. M. Mason*

984. **Paraffin-wax Baths in the Treatment of Rheumatoid Arthritis**
R. HARRIS and J. B. MILLARD. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 278–282, Sept., 1955. 8 refs.

An investigation is reported from the Devonshire Royal Hospital, Buxton, of the effect of paraffin-wax baths on the hands of patients with rheumatoid arthritis. A total of 90 patients were divided at random into 3 groups, one group receiving no local treatment for the hands, one receiving wax baths daily for 3 weeks, and one receiving wax baths daily for 6 weeks. All the patients were carrying out a general programme of rehabilitation and were taking 30 to 45 grains (2 to 3 g.) of aspirin daily. The hands were immersed repeatedly in melted wax, a glove thus being formed which was then covered with a layer of greaseproof paper for 20 minutes. After this, finger exercises were carried out. Skin temperature was recorded by means of a thermocouple inserted under the wax, and a cooling curve was plotted. Initially there was a rise in temperature of 2·9 to 9·5° C. (mean 5·8°), but in 10 to 60 minutes (mean 37 minutes) skin temperature was normal or below. The hands were examined before treatment started and thereafter at weekly intervals, and progress was assessed from objective criteria, including tenderness, pain, swelling, grip, and dexterity. It was found, however, that the progress indicated by these criteria was in close accord with the patient's subjective impression.

There was improvement in all 3 groups during the 6-week period as a result of rehabilitation, but there was little difference between the treated and untreated groups in respect of the local condition of the hands. The authors consider that paraffin-wax baths as employed in this investigation are of little value in the management of rheumatoid arthritis, but that further trial of the continuous immersion method is necessary before this form of treatment is discarded. *B. E. W. Mace*

985. **Electromyography as an Aid in Clinical Diagnosis**
P. A. SHEA and W. W. WOODS. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 787–793, Dec., 1955. 36 refs.

Neurology and Neurosurgery

HEREDITARY AND CONGENITAL DISEASES

986. **Huntington's Chorea: Results of Treatment with Reserpine**

J. A. LAZARTE, M. C. PETERSEN, C. W. BAARS, and J. S. PEARSON. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **30**, 358–365, Aug. 10, 1955. 2 figs., 9 refs.

Having observed that reserpine is effective in decreasing the physical activity of mentally ill patients, the authors considered that it might prove beneficial in the hyperkinetic states. Accordingly, at Rochester State Hospital, New York, 19 patients (10 males, 9 females) who had had symptoms of Huntington's chorea for periods ranging from 2 to 34 years were treated with reserpine for an average of 70 days. The drug was given in a dosage of 5 mg. intravenously on each of the first 3 days, followed, as a general rule, by 2 mg. by mouth twice a day, but the daily dose by mouth varied a little according to the clinical response, the maximum in some cases being 11 mg. Drugs of the amphetamine group were given to most of the patients to counteract the inertia resulting from the reserpine. The results of treatment were assessed from the clinical condition, from cinematographic recordings of the patients walking and at rest, and, in 6 cases, from ability to perform standard motor dexterity tests.

Hyperkinesis was appreciably decreased in all patients. Voluntary motor function improved in 18, and slight improvement in " emotional control " was noted in 12. Apart from some inertia due to reserpine no serious side-effects were observed, but shivering, salivation, intestinal motility, and vomiting occurred in 10 patients. The authors consider the treatment is purely symptomatic and its results transient. *L. A. Liversedge*

987. **Tabes of Friedreich with Degeneration of the Substantia Nigra, a Special Type of Hereditary Parkinsonism.** [In English]

A. BIEMOND and J. L. M. SINNEGE. *Confinia neurologica* [*Confin. neurol.* (*Basel*)] **15**, 129–142, 1955. 11 refs.

The authors describe, from the University Neurological Clinic, Amsterdam, 3 cases of Friedreich's disease with accompanying Parkinsonian symptoms occurring in a family in which 6 members belonging to three generations were known to suffer from a neurological heredo-degenerative disease. Only the present 3 patients, a man born in 1883, his daughter born in 1909, and his son born in 1925, could be examined. The remaining 3 affected members were known to have died in middle age after suffering for many years from an illness which started with walking difficulties and eventually led to total invalidism.

In the 3 cases described the illness started in the third decade of life, the initial picture being one of Parkinsonism, with or without absent tendon reflexes; this progressed slowly and was gradually modified by the appearance of ataxia and eventually of some muscular atrophy. The nosological classification of the disease was made difficult by the changing character of the clinical picture in each case, and also by the existence of extrapyramidal symptoms. It was only after a long follow-up and post-mortem studies (in one case) that a final diagnosis of Friedreich's ataxia was made.

The necropsy examination, made on the daughter, revealed marked demyelination of the spino-cerebellar tracts, mainly the ventral tracts, and to a lesser extent of the posterior columns of the cord. The majority of cells in Clarke's column had disappeared and the motor cells of the anterior horns showed degenerative changes. The substantia nigra of the midbrain had undergone considerable alteration, mainly in its cranial part, a large number of the cells having disappeared, while those that remained showed marked degenerative changes; these abnormalities were symmetrical. The remainder of the extrapyramidal system and the thalamus were normal. These pathological findings in the cord and cerebellum and some features of the clinical picture confirmed the diagnosis of Friedreich's ataxia. The atypical degeneration of the substantia nigra, which has not (so far as the authors know) previously been reported in conjunction with Friedreich's disease, would account for the Parkinsonian symptoms. *Richard de Alarcón*

988. **Neural Muscle Atrophy with Degeneration of the Substantia Nigra.** [In English]

A. BIEMOND and W. BECK. *Confinia neurologica* [*Confin. neurol.* (*Basel*)] **15**, 142–153, 1955. 9 figs., 10 refs.

An atypical heredo-degenerative nervous disease appearing in 3 members (2 brothers and one sister) of the same family is reported from the University Neurological Clinic, Amsterdam.

In the elder brother the disease started at the age of 48 with a distal atrophy of the limbs and minimal sensory disturbances; as the condition progressed he developed a bilateral Babinski response and eventually some extrapyramidal signs. In the younger brother the illness began at the age of 43 with a typical Parkinsonian syndrome which slowly progressed for some 10 years, at which time tendon reflexes were absent in the lower limbs and a right Babinski response was present; in this case there was no paresis, muscle atrophy, or sensory disturbance. The sister was married and had been healthy up to the age of 48 when paresis of the tibial muscles appeared, with absence of ankle-jerks and mild distal sensory disturbances. As the disease progressed a bilateral Babinski response and finally distinct Parkinsonian symptoms were noted. The clinical pictures were thus characterized by peripheral, pyramidal, and extrapyramidal symptoms, and the relative involvement of

each of these systems varied not only from patient to patient but also at different stages in the development of the illness in each case.

The elder brother died in 1952 and post-mortem examination revealed severe demyelination of the anterior spinal roots and less severe of the posterior roots. The cells of the grey matter of the cord were decreased in number and there was moderate demyelination of the fasciculus gracilis of the posterior column. Degenerative changes were found in both the nuclei hypoglossi and ambigui, and the substantia nigra appeared to be severely affected. In the cortex the giant cells of Betz in the precentral gyrus had almost entirely disappeared. In view of the pathological and clinical findings the authors concluded that neural muscular atrophy was the only possible diagnosis. The relationship between this disease and Friedreich's ataxia is discussed. The authors consider that the presence of Parkinsonian symptoms with degenerative changes in the substantia nigra, which they also found in 3 cases of Friedreich's ataxia [see Abstract 987] is another argument in favour of a close relationship between the two diseases.

Richard de Alarcón

BRAIN AND MENINGES

989. **A Method for the Quantitative Estimation of Papilloedema.** (Метод количественного измерения отечности соска зрительного нерва)

A. Y. Samoĭlov. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] **19**, 28–36, No. 5, Sept.–Oct., 1955. 4 figs.

The author describes a method for the measurement of papilloedema employed at the Burdenko Institute of Neurosurgery, Moscow. The elevation of the optic disk above the retina is estimated ophthalmoscopically and the width of the visual defect in the field of vision determined. Taken together, these figures provide a more rapid and accurate measurement of the degree of papilloedema than is possible by repeated subjective assessment.

L. Crome

990. **Hypertensive Cerebral Vascular Disease and Intracranial Tumour. A Study in Diagnosis**

A. Jefferson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 245–268, July, 1955. 5 figs., 24 refs.

The principal clinical features which are liable to lead to diagnostic confusion between hypertensive disease and intracranial tumour are headaches, abnormalities of the fundus oculi, abnormal pressure or protein content in the cerebrospinal fluid (C.S.F.), epileptic manifestations, and the development of focal intracranial neurological signs. In the study here reported from the Radcliffe Infirmary, Oxford, the clinical features in 69 cases of hypertension, in which an alternative diagnosis of cerebral tumour was considered, are compared and contrasted with those in 124 definite cases of intracranial tumour. The hypertensive cases were subdivided into two groups: (A) those with fundal changes (36) and (B) those without (33). There were 62 cases of meningioma and 62 of intrinsic brain tumour.

The symptom of headache was of no value in differentiating the two conditions. The C.S.F. pressure in the hypertensive patients, even without papilloedematous changes, tended to be above the average normal. The C.S.F. protein content was often as high as 100 mg. per 100 ml. in patients with hypertension, and in one case reached 200 mg. per 100 ml. for a time, although it fell after sympathectomy to 70 mg. per 100 ml. The average C.S.F. protein content in the hypertensive Group A was 63 mg. per 100 ml., and in Group B 69 mg. per 100 ml. The mean value in the two groups with tumour was rather higher, being 133 mg. per 100 ml. in the group of cases of meningioma and 109 mg. per 100 ml. in the other. The incidence of fits in the hypertensive patients was surprisingly high, 41% of them having a fit at some time in the evolution of their illness, though rarely as a presenting symptom. These convulsive attacks varied in pattern, but none was of the uncinate type, nor was there any petit mal. The epilepsy in these cases, however, appeared less " insistent " than in the tumour cases. Among other symptoms considered were mental and personality changes, vomiting, disturbance of gait, and the cardio-respiratory group of symptoms, such as dyspnoea, palpitations, ankle oedema, and angina pectoris. As might be expected, mental changes were more extensive among patients with tumour than in the hypertensive group, while the cardio-respiratory features were more prominent in the latter group. The other symptoms appear to have occurred more or less equally in the various groups. At times neurological symptoms may develop in patients with cerebral tumour with such suddenness as to suggest a vascular origin.

A review of the objective findings indicated the difficulty of differentiating the two groups on this basis. Thus pupillary abnormalities and all forms of motor, speech, and sensory deficit may appear as a result either of tumour or of hypertensive disease, but a high blood pressure associated with albuminuria strongly favours the diagnosis of hypertension. The electroencephalographic findings are discussed in respect of 39 hypertensive patients, 54 with meningioma, and 49 with intrinsic brain tumour. The author considers that this investigation may provide useful diagnostic information. Similarly, useful evidence regarding the presence of a tumour may result from plain radiographs of the skull, although it is noteworthy that erosion of the dorsum sellae and even deviation of the pineal gland may be found in certain patients with hypertension who have papilloedema. The special forms of radiological investigation, such as angiography, ventriculography, and lumbar encephalography are considered rather briefly and the attendant dangers mentioned.

The conclusion drawn by the author from this extensive review is that no single group of symptoms or of signs may be regarded as of absolute diagnostic value in differentiating hypertensive cerebral disease from intracranial tumour.

Fergus R. Ferguson

991. **The Intracranial Bruit**

I. Mackenzie. *Brain* [*Brain*] **78**, 350–368, 1955. 3 figs., 24 refs.

992. **Certain Disturbances of Attention Associated with Organic Cerebral Disease**
M. REINHOLD. *Brain* [*Brain*] **78**, 417–432, 1955. 6 refs.

In this paper from St. George's Hospital, London, the author defines attention as "a state of heightened or increased awareness of particular sensations". Awareness of sensation or perception is further defined as "the *qualitative* experience of a conscious person" accompanied or preceded by a sequence of events which include the reception, transmission, differentiation, and integration of sensory stimuli. The interrelation of psychological and physiological phenomena in regard to perception is demonstrated by reference to 2 cases of cerebral tumour involving the parietal region in which the patient's power of attention was disturbed.

The author amplifies a theory of sensory perception previously outlined (Gooddy and Reinhold, *Brain*, 1953, 76, 337) in which sensory stimuli are regarded as giving rise to patterns of nerve impulses which are fragmented, differentiated, circulated, and integrated in the nervous system. The physiological aspect of attention involves "the continued and intensified circulation and integration of particular patterns of nervous activity, with simultaneous diminution of co-existing other nervous activity". The psychological aspect of attention "includes the voluntary isolation and intensified awareness of particular sensations". From study of the 2 cases described it appeared that certain physiological factors such as the number of stimuli applied at any one time, "reinforcement" by other sensations, and repetition of stimuli are capable of influencing attention, so that inability to attend may be due to physiological as well as to psychological factors. *I. Ansell*

993. **Tumors of the Septum Pellucidum**
R. A. HUGHES, J. W. KERNOHAN, and W. M. CRAIG. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **74**, 253–258, Sept., 1955. 3 figs., 3 refs.

The authors suggest that tumours of the septum pellucidum are not so rare as has been thought, 57 cases of such tumours having been reported in the literature, to which they add 8 further cases. No clear-cut syndrome can be associated with these tumours, which seem to produce symptoms mainly by blocking the foramen of Monro; however, in 3 cases such well-marked ataxia was present that the cerebellum had been explored.
N. S. Alcock

994. **Caves and Cysts of the Septum Pellucidum**
R. A. HUGHES, J. W. KERNOHAN, and W. M. CRAIG. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **74**, 259–266, Sept., 1955. 5 figs.

Cavum septi pellucidi was found in 85% of 110 consecutive brains. The percentages were 89 for males and 80 for females. No correlation between incidence and age was noted. The embryology of the septum pellucidum is reviewed. It is pointed out that the cells lining the cavity of the septum pellucidum are possibly spongioblasts modified to resemble ependymal cells.—[Authors' summary.]

995. **The Repair of Dural Defects with Grafts of Umbilical Tissue in Cases of Fresh Cerebro-cranial Injury.** (Пластика дефектов твердой мозговой оболочки пластинками из ткани пуповины при свежей черепно-мозговой травме)
L. G. SHKOL'NIKOV and V. P. SELIVANOV. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] **19**, 54–58, No. 5, Sept.–Oct., 1955. 1 ref.

The authors have used preparations of umbilical-cord tissue to cover dural defects in 35 cases of cranial injury. The grafts are prepared in the following way. The umbilical cord is cut close to the placenta, cleared of blood by washing under running water, and placed in an aqueous solution of ammonia (1·5%) and formalin (1·5%), where it remains until all traces of colour disappear. It is then pressed to the thinness of paper, dried, and stored in alcoholic Lugol's solution, which is changed after a month. The graft is transferred before use to alcohol for 24 hours and to saline for a further 24 hours. The results are considered to be satisfactory and the method is recommended. *L. Crome*

EPILEPSY

996. **A New Method of Treatment of Epilepsy.** (Новый метод лечения эпилепсии)
M. Y. SEREĬSKIĬ. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 675–678, 1955. 3 refs.

The author discusses briefly the aetiology of symptomatic and idiopathic epilepsy and describes a method of control of the ictal phenomena with a combination of sedative, narcotic, and stimulant drugs. Three formulae containing phenobarbitone, "bromural" (bromvaletone) caffeine sodium benzoate, papaverine, and calcium gluconate in varying proportions are given, and the theoretical reasons for the efficacy of the combination, in terms of the influence on cerebral physiology of the various components, are expounded at some length, supported by experimental findings.

Indications for the clinical use of each of the three formulae are given, and it is claimed that excellent results have been obtained from the extensive application of the method over a period of 3 years in a number of hospitals and clinics [but apart from some references to the published work of other Russian clinicians using the formulae, the author gives no details on which a comparison with other established methods can be based].
Alexander Duddington

997. **A Trial of Sereĭskiĭ's Formula in the Treatment of Epileptic Children.** (Опыт лечения больных эпилепсией детей смесью Серейского)
M. A. USPENSKAYA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 679–681, 1955.

The claim of Sereĭskiĭ [see Abstract 996] that the use of a number of synergistic drugs in combination gives better control of the symptoms of epilepsy than can be obtained with any one of them alone is supported

by the author's experience in the treatment of 48 epileptic children over a period of 2 years with Sereĭskiĭ's formulae. Treatment of the underlying pathological lesion, where appropriate, was carried out in the same way as in previous groups which had received different symptomatic treatment, so that a comparison of results was possible. Fairly full clinical details of the experimental group and of the changes observed under treatment are given. The best results were obtained in cases with major fits or abortive attacks of various types, whereas in cases of petit mal there was little or no effect. [No reference to electroencephalographic studies is made.]

Alexander Duddington

998. **Mesantoin in the Treatment of Epilepsy**

R. A. WISE and W. A. HEUMANN. *Psychiatric Quarterly* [*Psychiat. Quart.*] **29**, 403–411, July, 1955 [received Nov., 1955]. 7 refs.

The effects of treatment with " mesantoin " (methoin) on 100 patients aged from 4 to 71 years suffering from symptomatic and idiopathic epilepsy of various clinical types are described from Craig Colony Hospital, New York State. In all cases the drug was combined with phenobarbitone. No significant effect was observed on seizures of the petit-mal type or on myoclonia, but of the patients with grand mal the seizures were totally abolished in 14%, greatly reduced in number in 68%, but increased in number in 17%. Contraindications and adverse reactions to mesantoin therapy are discussed. The authors conclude that this drug is of value in cases of grand mal which appear refractory to other anticonvulsants, but that careful attention is essential to avoid the possibility of serious toxic reactions and haematological changes.

J. B. Stanton

CRANIAL NERVES

999. **Stilbamidine Isethionate Therapy of Tic Douloureux**

B. WOODHALL and G. L. ODOM. *Journal of Neurosurgery* [*J. Neurosurg.*] **12**, 495–500, Sept., 1955. 27 refs.

As a consequence of the observation of Napier and Sen Gupta that a late chronic neuropathy, confined largely to the distribution of the fifth nerve, sometimes occurred as a sequel to the administration of stilbamidine to patients with kala-azar, the authors have employed this drug at Duke University Hospital, Durham, N. Carolina, in an attempt to control the pain of tic douloureux in 41 patients (15 male and 26 female). Stilbamidine isethionate in a course of 10 injections to a total of 1·5 g. of the drug was given in daily doses of 0·15 g. freshly dissolved in 150 ml. of 5% glucose and distilled water by intravenous infusion over a period of one hour.

In 36 of the 41 patients there has been relief from pain for periods of from 9 months to 2 years; the relief has been associated with sensory changes over the trigeminal and upper cervical dermatomes, suggesting the development of a true chemical neuropathy. In a small proportion of the cases unpredictable formication and paraesthesia occurred over the face. The delayed action of the drug in patients with severe pain may necessitate provisional methods of control before the onset of the chemical neuropathy. As the authors point out, however, the notorious tendency for the pain of tic douloureux to vary considerably in intensity makes any real analysis of the early effects of this drug unreliable. Some patients did have slow remission of pain in the latter part of the course of treatment, but in most cases lasting relief did not set in until after 40 to 150 days, and was usually followed rapidly by the onset of the characteristic neuropathy.

These observations would appear to encourage a continuing study of the influence of stilbamidine by both intravenous and oral administration upon the course of this disease.

D. P. McDonald

1000. **Late Results of Facial Nerve Repair**

R. C. MARTIN. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **64**, 859–869, Sept., 1955. 6 figs., 8 refs.

In this paper from the University of California the late results of facial nerve repair carried out 18 to 26 years previously are reported. Muscle tone was good, but voluntary motor control was never quite complete, being absent from the frontalis muscle. Associated movements were least obvious in cases in which end-to-end anastomosis was performed and more marked after a nerve graft. Contractures and tics usually disappeared in 2 to 5 years. In patients subjected to end-to-end anastomosis there was improvement over the years, but in those subjected to nerve graft there was seldom any progress after the first year.

William McKenzie

SPINAL CORD

1001. **Nutritional Spinal Ataxia**

G. L. MONEY and A. S. SMITH. *West African Medical Journal* [*W. Afr. med. J.*] **4**, 117–123, Sept., 1955. 14 refs.

In this paper from University College Hospital, Ibadan, Nigeria, 4 cases of spinal ataxia attributed to nutritional deficiency are described, the patients being 2 males, aged 20 and 50 years, both labourers, and 2 females, a housewife aged 22 and a schoolgirl aged 12. The earliest subjective symptoms were paraesthesiae and blurring of vision. Visual impairment was severe in 3 of the patients (6/60 by Snellen's types) and moderate in one patient. The neurological signs indicated degeneration of the posterior columns. Gait was tabetic with foot drop, the tendon reflexes were depressed or absent, and the plantar response was flexor. Bitemporal pallor of the optic disks was noted. In all cases the results of serological tests were negative, the cerebrospinal fluid was normal, and free hydrochloric acid was present in the resting gastric juice. The authors briefly describe the diet of these patients, which consisted mainly of cassava and yams; the protein content was low. Treatment consisted in an adequate diet supplemented by vitamins of the B complex, including cyanocobalamin. Although some improvement was noted, the neurological changes were in the main irreversible.

William Hughes

1002. **Acute Necrotic Myelopathy**
H. L. HOFFMAN. *Brain* [*Brain*] **78**, 377–393, 1955. 3 figs., 42 refs.

The author gives details of 3 fatal cases of acute necrotic myelopathy, with the necropsy findings, and describes the cases of 2 further patients with a similar clinical picture who survived, all 5 cases occurring in hospitals of the Bath group. These patients developed flaccid paralysis of the lower limbs, with complete sensory loss, which ascended to the thoracic region or higher over a period of several days. Sphincter control was lost, and there was no recovery of function in the cord below the upper level of the lesion. Changes in the cerebrospinal fluid were inconstant, the protein content ranging from 33 mg. to 450 mg. per 100 ml. and the cell count from 22 to 4,016 per c.mm., with occasional xanthochromia. At necropsy the meninges appeared normal and the blood vessels were neither thrombosed nor sclerotic. The cord was oedematous and in parts necrosed. Histological examination revealed demyelination and foci of necrosis, especially in the posterior columns. In more than one-third of cases no significant change was found in the intra- or extra-medullary blood vessels; where such changes were present it was considered that they were not responsible for the necrosis, but represented a simultaneous response to some common toxic or infective agent.

The author discusses the nature of the infection which precedes the onset of necrotic myelopathy in about one-third of all reported cases, and points out that this disease is usually associated with a bacterial infection, whereas disseminated encephalomyelitis more often follows infection with a non-neurotropic virus. In view of the danger of causing a spread of bacterial infection, which apparently occurred in one case in the series, treatment with ACTH or cortisone should be undertaken with the greatest caution.

The association of acute necrotic myelopathy with malignant neoplasms outside the nervous system, which has been noted in a few cases, was not observed in the present series. *I. Ansell*

DISSEMINATED SCLEROSIS

1003. **Treatment of Multiple Sclerosis with Low-fat Diet**
R. L. SWANK. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 631–644, June, 1955. 1 fig., 41 refs.

During the past 5½ years 158 out of 264 patients attending the Montreal Neurological Institute suffering from disseminated sclerosis have been treated with a low-fat diet. Detailed results are here given for 44 of these patients who have been followed up for at least 4 years while continuing to take the diet. In a large proportion of cases the frequency and severity of exacerbations of the disease steadily decreased during this period, the number of exacerbations per year being less than that during the 3 years before starting the diet by an average of 0·76, this difference being highly significant statistically. The effect of the diet varied widely in different patients (from an increase of about 0·5 episode per year to a decrease of 3·6 per year) and no benefit was observed in 2 cases of the progressive type with no exacerbations. *Donald McDonald*

1004. **Antibrain Antibodies in Multiple Sclerosis**
N. RASKIN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 645–655, June, 1955. 1 fig., 24 refs.

An investigation is reported from the Boston State Hospital, Dorchester, Massachusetts, into the hypothesis that disseminated sclerosis is of an allergic nature and that the serum of patients suffering from the disease may contain antibodies to antigens arising in the brain. Complement-fixation tests were performed on serum from 120 patients with the disease and 60 control subjects with six different antigen fractions prepared from brains affected by disseminated sclerosis. The first three were derived from an acetone extract of brain and the others from the alcohol-soluble fraction.

Altogether, positive reactions were obtained in 83·3% of the tests on patients' sera and in only 42·6% of those on the controls' sera, a statistically significant difference with a probability of less than 0·01. In individual patients the activity of the test appeared to bear no relation to the duration of the illness or to its severity. Some of the normal sera neutralized the complement-fixing antibodies in sera from cases of disseminated sclerosis; hence the therapeutic effect of transfusions of such normal blood is being studied.

Donald McDonald

1005. **Intellectual and Affective Functions in Multiple Sclerosis**
A. T. ROSS and R. M. REITAN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 663–677, June, 1955. 4 figs., 43 refs.

Standard methods of measurement of intelligence in patients with disseminated sclerosis do not usually show any impairment of intellectual function. In the investigation reported here from Indiana University Medical Center, Indianapolis, the authors applied Halstead's tests for measurement of biological intelligence, which were specifically designed to detect intellectual deterioration due to organic cerebral damage, the Minnesota Multiphasic Personality Inventory, and the Rorschach test to each of 13 patients with disseminated sclerosis and compared the results with those obtained in two carefully matched control groups, one of 13 patients known to have organic brain damage and the other of 13 subjects without such damage.

The results of the Halstead tests indicated a severe and similar degree of intellectual impairment in many of the patients with disseminated sclerosis and of those with organic brain damage, whereas the results in the group without organic brain damage were within normal limits. The Minnesota personality tests gave very similar results in all three groups, while the results of the Rorschach test indicated a slight and similar degree of impairment in the first two groups and were within normal limits in the third. *Donald McDonald*

Psychiatry

1006. **Release of Cyclothymic Depression by Psychological Events.** (Über Auslösung cyclothymer Depressionen durch seelische Erschütterungen)
H. KORNHUBER. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **193**, 391–405, 1955. Bibliography.

The author found adequate evidence of the release of a depressive psychosis by emotional events in 22 out of 300 women and in 17 out of 300 men suffering from endogenous affective psychoses studied at the Psychiatric Clinic of the University of Heidelberg. In an equal proportion of cases the depression was provoked by some physical illness or trauma, and in a similar number of cases it started during childbirth or in the puerperium. The author considered the patients in whom the illness was provoked to be less tainted by hereditary factors than those in whom it arose spontaneously. He also gives criteria for the differentiation of provoked endogenous depression from depressive reactions of a neurotic nature. While provoked depression is, as seen in his material, a response to disturbing events arising suddenly, neurotic depressive reactions follow persistent and long-standing emotional stress.

[The inquiry was made with great care and the conclusions are based on intensive study of all the case histories, many of the patients being seen by the author personally. It bears the stamp of critical scrutiny and restraint characteristic of the Heidelberg School.]

W. Mayer-Gross

1007. **Suavitil in the Treatment of Psychoneuroses**
O. Ø. JENSEN. *Danish Medical Bulletin* (*Dan. med. Bull.*) **2**, 140–143, Sept., 1955. 6 refs.

" Suavitil " (benactyzine; diethylaminoethyl benzilate) was used at the Danish Red Cross Sanatorium, Hald, in the treatment of psychoneurosis in 44 male patients (average age 40 years, range 16 to 75) and 66 female patients (average age 39, range 15 to 76), 96 of whom were in-patients. A control group made up of 110 patients attending the hospital during the same period and picked at random, but representing approximately the same types of case, were given routine treatment with thiopentone or phenobarbitone. The results were assessed as " good " if practically all the neurotic symptoms disappeared and those remaining were only slightly disturbing, and as " moderate " if, although the more important neurotic disturbances were abolished, some disturbing symptoms remained. Each assessment was based on the patient's statements, on the doctor's impression of his willingness to accept a psychotherapeutic explanation and to cooperate in therapy, and on the nurses' report on his behaviour in the ward.

After 3 weeks' treatment with various doses of benactyzine the results were good in 56 cases and moderate in 19, no definite effect being noted in 35. The corresponding figures for the control group were 25, 28, and 57 cases respectively. The longer the illness, the poorer the results seemed to be, the effect of benactyzine being considerably less when persistent insoluble problems were present. In the absence of such problems there was no significant difference between the results in patients with and without a history of psychic trauma. Psychoneurotic disorders with anxiety, those with neurotic depression, and to a lesser extent those with obsessive–compulsive reactions or asthenic reactions seemed to be influenced by benactyzine. Four patients with endogenous depression did not respond, but 5 others with psychoneurosis in a depressive constitution seemed to respond well. A tendency to speculate and ruminate seemed to be affected especially early and favourably. When placebo tablets were given to 40 patients who had responded to benactyzine all but 2 relapsed, but responded at once when the drug was given again.

Only a few patients responded to a dosage of 0·5 mg. 3 times a day, while 1·5 mg. had little more effect than 1 mg. 3 times a day, though the higher dose caused blocking of the thoughts in a few cases. Otherwise only a few insignificant side-effects—slight dizziness and feelings of " queerness "—were reported. Of the 14 ambulant patients (mainly cases of neurotic–depressive reaction), a good result was obtained in 11. Ten of the in-patients continued to take the drug after leaving the sanatorium, with good effects. *John C. Kenna*

1008. **An Evaluation of Subcoma Insulin Therapy**
D. C. GREAVES, P. F. REGAN, and L. J. WEST. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **112**, 135–139, Aug., 1955. 11 refs.

Subcoma insulin therapy was given as an adjuvant to psychotherapy to 159 patients (133 suffering from schizophrenia and 26 from affective disorders) at the Payne Whitney Psychiatric Clinic, New York Hospital. The authors state that patients suffering from manic excitement or depression were given this treatment only when anxiety was a prominent feature; similarly, psychoneurotics were treated when cachexia or debilitation was present, or " thinking difficulties " related to anxiety made psychotherapy ineffectual. Patients received insulin in a dosage of 20 to 200 units and were kept for 45 to 60 minutes in the " precoma " phase of clouded consciousness in which there is barely any response to strong noxious stimuli. A total of 50 to 60 effective subcoma treatments were given. Criteria of improvement were subjective relief of distressing symptoms, improved " thinking " and concentration, and less disturbed behaviour.

Of the schizophrenics, 106 improved including 53 (out of 64) of the paranoid type, 34 (out of 43) of the catatonic type, and 19 (out of 26) of other types. In the paranoid group the percentage improvement was higher in those suffering from acute or subacute disturbances, with fear, incoherence, elation, or depression, than in those with a

gradually developing disturbance. In the catatonic group improvement was obtained in all 12 patients with fear and severe anxiety, in 3 out of 7 in whom anger was predominant, and in 10 out of 12 with stupor associated with fear or depression.

Of the patients with affective disorders those showing elation and anger, sexual excitement, resentment, and panic responded well, but in contrast to the schizophrenic group, the response of those with fear and severe anxiety was less satisfactory.

In conclusion the authors point out that coma or subcoma insulin therapy is not specific for schizophrenia or affective disorders, but is useful for the relief of many distressing symptoms and facilitates psychotherapy and subsequent readjustment. *Richard de Alarcón*

1009. **An Evaluation of Carbon Dioxide Therapy**
A. A. LAVERNE amd M. HERMAN. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **112**, 107–113, Aug., 1955. 16 refs.

Carbon dioxide inhalation therapy has been employed over the past 3 years in the treatment of patients at the Bellevue Psychiatric Hospital, New York, and in this paper the authors review the results obtained in 133 patients suffering from a wide variety of conditions, including anxiety neurosis, conversion hysteria, neurotic homosexuality, obsessive–compulsive neurosis, neurotic and psychotic depression, alcohol and drug addiction, schizophrenia, cerebral palsy, and even dystonia musculorum (2 cases). Both Meduna's slow-coma technique with 30% CO_2 in an oxygen mixture and the rapid-coma technique with high concentrations (70 to 80%) of CO_2 were used. On the whole, better results were obtained with the latter than with Meduna's technique, even in those cases which, according to the criteria of Meduna, were most suitable for treatment by the slow-coma method. Of the neurotic group only 22% improved with Meduna's method compared with 50% of those treated by the rapid-coma technique. The latter also proved successful in 7 out of 15 obsessional neurotics and 8 out of 24 schizophrenics. To the known contra-indications to this form of treatment the authors add respiratory sensitivity, which is characterized by the development of apnoea after the first inhalation.

Discussing complications the authors state that in 3 neurotic patients anxiety developed into a panic state bordering on an acute psychosis, and in one neurotic and two borderline psychotic patients a gross psychosis was precipitated by the treatment. Treatment anxiety was frequently encountered; this complication calls for careful management because the patient may interrupt treatment or the condition may be aggravated; this complication, if neglected, may make the "cure" worse than the disease. The authors emphasize the hazards associated with induction of very deep coma; in their view subcoma is the safest and most effective level when the rapid technique is used.

[No qualitative assessment of the improvements obtained is given, nor is there any definite indication of the type of patient for whom this treatment is most suitable.] *Richard de Alarcón*

1010. **Observations during the Treatment of 175 Psychotic Patients with Reserpine**
R. B. FREUND. *Psychiatric Quarterly* [*Psychiat. Quart.*] **29**, 381–389, July, 1955 [received Nov., 1955]. 4 refs.

The author presents clinical observations on the use at Utica (New York) State Hospital of reserpine in the treatment of 175 psychotic patients who were selected on account of symptoms of disturbed behaviour, hyperactivity, or catatonic stupor rather than of the type of psychosis. In general the use of reserpine in this group abolished the necessity for electric convulsion therapy and insulin treatment. It was noted that during treatment with the drug patients passed through three consecutive stages, first one of sedation, then one of disturbance with exaggeration of secondary symptoms, and finally an integrative phase when they became accessible to and likely to benefit from psychotherapy. In some cases the response was enhanced by giving the drug in repeated courses with short intermissions. Patients who had previously received several courses of physical treatment or who had undergone lobotomy without beneficial effect did not go successfully through the three stages mentioned above, while only tranquillizing effects were obtained in organic cases. Side-effects, especially hypotensive symptoms, were virtually absent. The re-orientation in the attitude of mind among mental hospital staff and in administration which the successful and more widespread use of reserpine may require in the future are discussed. *J. B. Stanton*

1011. **Preliminary Report on 500 Patients Treated with Thorazine at Rochester State Hospital**
B. POLLACK. *Psychiatric Quarterly* [*Psychiat. Quart.*] **29**, 439–456, July, 1955 [received Nov., 1955].

The response of 170 male and 330 female patients to treatment with "thorazine" over periods varying from one to 9 months at Rochester State Hospital, New York, is described. Patients selected for treatment were those who showed "mobile emotion", that is, anxiety, fear, aggression, excitement, depression, and hypochondria. The drug was given orally in doses of between 100 and 600 mg. daily or intramuscularly in doses of 100 and 400 mg. daily. Elderly patients were given smaller doses and kept in bed for the first few days of treatment whenever possible.

An obvious improvement in behaviour was noted in 74% of the whole group, in 85% of manic–depressive patients, and 67% of schizophrenic patients. The degree of improvement in the psychotic condition was estimated at 60% for the whole group, ranging from 80% for manic–depressive psychosis to 33% for schizophrenia. In most of the psychotic cases thorazine appeared to be as effective as electric convulsion therapy, which it could replace.

Of 85 patients who had previously required restraint or seclusion, 42 became so much better with thorazine treatment that they could be released. Out-patients were also treated with good effect. Side-effects of the treatment and the ancillary measures likely to assist in obtaining the best results in patients under thorazine treatment are described. *J. B. Stanton*

Dermatology

1012. **Liquid Nitrogen Therapy in Dermatology**
I. ZELIGMAN and H. M. ROBINSON. *Bulletin of the School of Medicine, University of Maryland* [*Bull. Sch. Med. Maryland*] **40**, 132–134, Oct., 1955. 2 figs., 6 refs.

At the University of Maryland School of Medicine, Baltimore, liquid nitrogen was used in the treatment of 512 patients with warts of various types. Into the liquid nitrogen, which was obtained in litre vacuum flasks, absorbent cotton rolled on an applicator stick was dipped, the liquid being then allowed to drip on to the lesion until it turned white, no pressure being used. There was usually a burning sensation for some hours and subsequent vesicle formation. The lesions then dried and peeled off within one to 3 weeks. Excellent results were obtained in 456 cases, one application being sufficient for small verrucae. Plantar warts, however, did not respond well, only 3 of 9 cases being successful. Liquid nitrogen was also tried in 12 cases of seborrhoeic keratosis, all of which responded well, an excellent cosmetic result being obtained.

The authors have found this method of treatment more successful than any other for periungual warts. Liquid nitrogen has an advantage over oxygen in that it is more easily obtained and does not support combustion, and over carbon dioxide snow in that it does not need pressure application, which has the disadvantage of being difficult to gauge accurately. *E. H. Johnson*

1013. **Treatment of Lupus Vulgaris with Calciferol Alone. Results after Five Years of Observation**
P. V. MARCUSSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **2**, 129–136, Sept., 1955. 5 figs., 18 refs.

A series of 284 patients suffering from lupus vulgaris and treated at the Finsen Institute, Copenhagen, with calciferol alone have been kept under observation for 7 to 9 years. The calciferol was given in a dose of 4·5 mg. (180,000 units) daily for 3 weeks, after which the dose was adjusted according to the patient's tolerance. The treatment was, so far as possible, continued until there had been clinical and pathological evidence of cure for at least one year, or until a total dose of not less than 1 g. of calciferol had been given.

Of the 284 patients, 271 completed the course of treatment and 223 (78·5%) became symptom-free; of these, however, 120 showed a relapse at the conclusion of the observation period, 83 remained free of disease, and the remainder had died or were lost to follow-up. Of the then available patients, 101 received a second, 23 a third, and 2 a fourth course of treatment, the cure rate falling to 45·5% and 30·4% for the second and third courses respectively. The relapse rate was high.

Toxic effects of calciferol were seen and 85 patients showed clinical signs of intolerance of the drug.

[This paper contains much information and should be read in full by those interested.] *S. T. Anning*

1014. **Topical Anticholinergic Therapy—Prantal Cream in the Treatment of Dermatoses: a Preliminary Report**
H. M. ROBINSON. *Bulletin of the School of Medicine, University of Maryland* [*Bull. Sch. Med. Maryland*] 40, 128–131, Oct., 1955. 13 refs.

The author describes the results of a trial in private practice and at the University of Maryland Dermatological Clinic, Baltimore, of 2% "prantal" cream, a preparation containing 20 mg. of diphemanil methylsulphate per g., as a topical anticholinergic in 107 patients. The various dermatoses treated included 67 cases of contact and/or eczematous dermatitis, 31 of eczema, 3 of dermatitis venenata, 2 of onychia, and one each of folliculitis, lupus erythematosus, psoriasis, and scleroderma. The cream was lightly applied three times daily.

In 42 out of the 107 patients the skin condition healed or improved markedly in 2 weeks, in 16 in 1 to 3 months, and 22 patients are progressing satisfactorily with continued treatment. Failure to improve occurred in 7 cases of dermatitis, 6 of eczema, and also in the cases of lupus and psoriasis. In 15 cases patients with symmetrical lesions applied only the cream base on one side as a control; no improvement occurred on that side. No systemic side-effects were recorded, but 12 patients complained of a burning irritation and treatment was discontinued. The outstanding effects of the treatment were the immediate relief from pruritus, and the anhidrotic action of the cream. *E. H. Johnson*

1015. **Dermatitis Herpetiformis (Duhring) Successfully Treated with Promacetin**
M. J. COSTELLO and C. M. BUNCKE. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **72**, 348–352, Oct., 1955. 7 refs.

The effect of "promacetin" ("acetosulphone"; sodium 2-N-acetylsulphamyl-4:4′-diaminodiphenylsulphone) in the treatment of 12 patients suffering from dermatitis herpetiformis (Duhring's disease) is discussed in this paper from Bellevue and St. Clare's Hospitals, New York. It was found to be second only to sulphapyridine in efficacy and had the advantage of being much less toxic. Because there is the risk that agranulocytosis may develop with this treatment, the authors emphasize the need for repeated estimation of the leucocyte count during the first month. They state that since iron-deficiency anaemia develops in patients given prolonged treatment with promacetin it is advisable to administer an iron preparation at the same time. Scarlatiniform and morbilliform rashes and mild nausea and headache occurred in some cases. To achieve a remission a daily dose of 3 to 4 g. was necessary, the maintainance dose usually being 2 to 3 g. daily. In some cases a combination of relatively small doses of promacetin and sulphapyridine was more effective than promacetin alone. *E. Lipman Cohen*

Paediatrics

1016. **Children Who Take No Cod Liver Oil**
W. T. C. Berry, K. M. B. Boyes, W. C. Parr, and K. F. Smith. *Monthly Bulletin of the Ministry of Health* [*Monthly Bull. Minist. Hlth (Lond.)*] **14**, 162–165, Oct., 1955. 10 refs.

Doubt having been expressed by members of the Child Health Panel for Salford, Lancashire, concerning the nutrition of children aged 1 to 2 years, an investigation was undertaken to determine whether these children were suffering from deficiency of calciferol. In a group of 37 children aged 12 to 25 months, 27 of whom had never received cod-liver oil and 10 had received a minimal amount, the diet, rate of growth, the level of tooth eruption, and the radiological appearances of the wrist were studied and the serum alkaline-phosphatase and haemoglobin levels were determined; a group of 50 children of similar age who were known to have received adequate supplements of cod-liver oil served as controls. Growth and general conditions were poorer in the study group than in the controls, but this was thought to be due to conditions other than lack of calciferol; apart from this no differences were observed between the two groups. It was apparent that the study group received sufficient calciferol from dried milk and other sources. The authors suggest that if the diet contains enough calciferol the addition of cod-liver oil may lead, in some instances, to ingestion of toxic amounts of the vitamin; they discuss this possibility in the light of reports of hypercalcaemia in bottle-fed infants.

I. A. B. Cathie

NEONATAL DISORDERS AND PREMATURITY

1017. **Haematogenous Osteitis in the Newborn**
W. M. Dennison. *Lancet* [*Lancet*] **2**, 474–476, Sept. 3, 1955. 3 figs., 18 refs.

Effective antibiotic therapy of septicaemia in the newborn has greatly improved the prognosis in this condition, and more infants are surviving long enough to show clinical evidence of haematogenous osteitis. Since 1945, 41 cases of neonatal osteitis have been admitted to the Royal Hospital for Sick Children, Glasgow, and in this paper the treatment is discussed. Cases were classed as "benign" or "severe" (but the inadequacy of such a grouping was clearly recognized). In most of the 22 benign cases the infecting organism was a staphylococcus and the commonest foci were the maxilla (8 cases), humerus (5), and femur (4). Most organisms were resistant to penicillin, but permanent bone destruction and subsequent deformity occurred only in 6 cases, either the humerus or the femur being involved.

Of the 19 infants with severe neonatal osteitis, 4 died and in the remainder recurrent infection, the formation of sequestra, and extensive bone destruction produced a high morbidity rate. Multiple lesions were present in many of these cases. The commonest infecting organism was again a staphylococcus, which in nearly all the cases was penicillin-resistant. [This is in marked contrast to the penicillin-sensitive organism which affects patients in older age groups.] Although aureomycin controlled the toxaemia, it appeared to have little effect upon the bone lesion, metastatic foci developing during treatment or a relapse occurring soon after the drug was withdrawn. In the most recent cases of severe neonatal infection a penicillin–streptomycin preparation was used, which proved to be as effective as aureomycin in the control of toxaemia. The author emphasizes, however, that whichever antibiotic is used treatment should cease as soon as the haematogenous infection is under control.

Peter Ring

1018. **Effect in the Newborn Infant of Reserpine Administered ante Partum**
I. S. Budnick, S. Leikin, and L. E. Hoeck. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **90**, 286–289, Sept., 1955. 6 refs.

Nasal stuffiness or "congestion" is known to be a side-effect of reserpine therapy. At the District of Columbia General Hospital, Washington, the authors, having observed that a number of infants had nasal discharge shortly after birth, studied all cases of this condition occurring over a 3-month period with the object of determining the aetiological factor. During this period reserpine was being used in the obstetric department of the hospital in the treatment of hypertension in association with toxaemia of pregnancy.

It was found that in 12 of the 77 infants born to mothers receiving such treatment there were toxic symptoms, consisting in watery or mucoid discharge, followed by obstruction to respiration, with rib retraction and cyanosis. The infants were lethargic and poor feeders, but no gastro-intestinal disturbance was observed. In the main these toxic reactions were self-limited, lasting one to 5 days. There were two deaths in the series, one of which appeared to be due to the toxaemia. It is suggested the symptoms are either a manifestation of a drug sensitivity peculiar to the newborn or the result of rapid concentration of the drug in the placenta.

Winston Turner

1019. **Protein Catabolism and Renal Function in the First Two Days of Life in Premature Infants and Multiple Births**
R. A. McCance and E. M. Widdowson. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 405–409, Oct., 1955. 13 refs.

The authors report, from the University of Cambridge, the results of a study of renal function in 2 premature male infants, four pairs of twin boys, and one set of triplets. In all cases labour had been normal and the weights of the infants ranged from 1·08 to 2·5 kg.

The triplets, who were scarcely of viable age, all died but the other 10 babies progressed satisfactorily. In 6 out of the 10 surviving infants the serum urea level fell during the second 24 hours of life, and it is concluded that in these premature children the kidneys were fully as capable of dealing with the demands made upon them as were those of normal full-term babies. It is suggested that toxaemia of the mother may impair maternal but not infantile renal function, whereas a prolonged and difficult labour may, temporarily at any rate, impair the renal function of both mother and child.

The composition of the urine of the 10 thriving premature babies, as judged either by the amounts of the various constituents present per litre or by their contribution to the total osmolar concentration, differed little from that of normal full-term babies or of " distressed " babies. The concentration of inorganic phosphorus found in the maternal and cord serum and the total amounts of phosphorus excreted on the first and second days of life by the infants were within the normal range. This admittedly small study seems to show that infants of multiple births and premature infants over the first 48 hours of life exhibit renal function in no way inferior to that of normal full-term infants.

J. M. Smellie

CLINICAL PAEDIATRICS

1020. Portal Hypertension in Infants and Children

D. Yi-Yung Hsia and S. S. Gellis. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **90**, 290–298, Sept., 1955. 37 refs.

An analysis is presented of all cases (43) of portal hypertension in infants and children seen at the Children's Medical Center, Boston, in the 30-year period 1924–53. It is pointed out that primary portal hypertension is manifested by splenic enlargement, with hypersplenism, dilated collateral oesophageal varices, and haemorrhage; there are no signs of liver damage. A history of omphalitis or of other severe infection in early infancy is often elicited in such cases. Of the 43 patients, 21 had primary portal hypertension and 22 had portal hypertension secondary to cirrhosis of the liver. Hepatitis appeared to be the commonest aetiological factor in the latter group of cases, in many of which liver function was abnormal. Since there is little effective medical treatment for secondary portal hypertension the authors recommend establishment of a venous shunt; a splenorenal shunt is the procedure of choice but if this is not possible a porto-caval shunt should be performed.

Winston Turner

1021. Hypertrophic Pyloric Stenosis in Infancy Treated with Methyl Scopolamine Nitrate

B. D. Corner. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 377–386, Aug., 1955. 4 figs., 20 refs.

The author reports, from Bristol Royal Hospital for Sick Children, the results of treating 117 cases of congenital hypertrophic pyloric stenosis with methyl scopolamine nitrate (" skopyl "). There were 93 males and 24 females and in all but 9 cases the onset of symptoms occurred before the age of 7 weeks. Treatment consisted in immediate admission to hospital, wash-out of the stomach, a special feeding schedule of the " ladder " type, and administration of skopyl in a dose of 0·1 mg. by mouth 15 minutes before the feed six times daily. Parenteral fluids were given when necessary and in some cases skopyl was administered subcutaneously in a dose of 0·05 mg.

All the babies except 2 made a rapid recovery; one infant died, and another after 19 days was treated surgically (Ramstedt's operation) and then recovered. There were no signs attributable to any toxic action of the scopolamine. Two patients developed upper respirafory tract infection and one, who was nursed in a general children's ward, developed gastroenteritis. It is concluded that skopyl is a safe and very effective drug for the treatment of congenital hypertrophic pyloric stenosis, but that a restricted diet is necessary initially. The importance of isolation and special nursing care is stressed.

Kathleen M. Lawther

1022. Rectal Biopsy as an Aid in the Diagnosis of Hirschsprung's Disease

O. Swenson, J. H. Fisher, and H. E. MacMahon. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 632–635, Oct. 13, 1955. 6 figs., 3 refs.

The authors, working at Tufts University School of Medicine, Boston, have found that rectal biopsy is a useful diagnostic aid in cases of Hirschsprung's disease in which the clinical and radiological findings are inconclusive; it was carried out by them in 40 out of 169 patients with congenital megacolon. Case histories are given to illustrate the main indications for this procedure, which are as follows. (1) Cases in which colostomy has previously been carried out and which therefore do not show a dilated colon with a narrow distal segment on radiography. (2) In the newborn: as the colon does not become dilated and hypertrophied until it has been functioning for several months, Hirschsprung's disease in the newborn may present as upper large-bowel obstruction. (3) In those cases of the disease in which the narrow segment is short and so low that it cannot be demonstrated radiologically. (4) In cases in which megacolon is present with atypical symptoms such as diarrhoea or episodes of intestinal obstruction.

In all such cases rectal biopsy was carried out and was effective in confirming or excluding the diagnosis of Hirschsprung's disease by demonstrating the presence or absence of myenteric ganglion cells. The biopsy is carried out under general anaesthesia, a 1-cm. longitudinal incision beginning at Hilton's line being made through the anal mucosa and carried up between the columns of Morgagni. The mucosa is lifted by blunt dissection and a segment of internal sphincter muscle 5 to 10 mm. in length and extending into the rectum is excised, care being taken to include both circular and longitudinal muscle fibres between which the ganglion cells lie; troublesome bleeding is controlled by fine chromic-catgut sutures along the cut mucosal edge. Of the 40 patients thus investigated, 19 were found to have

Hirschsprung's disease—confirmed later by a study of the excised rectum—and 21 had chronic constipation which responded well to conservative treatment.

F. Hillman

1023. Intramuscular Iron in Infancy

W. Gaisford and R. F. Jennison. *British Medical Journal* [*Brit. med. J.*] **2**, 700–704, Sept. 17, 1955. 7 figs., 15 refs.

The intravenous administration of iron to children is difficult and, according to published reports, gives rise to thrombosis, syncope, or other side-effects in about 10% of cases. At the Royal Manchester Children's Hospital and St. Mary's Maternity Hospital, Manchester, about 100 babies and children have been treated with good results for anaemia (nutritional, of prematurity, or after haemorrhage) with a new, non-irritant preparation, "imferon", which is an iron–dextran complex containing 50 mg. of elemental iron per ml. All the patients responded well, and there was no skin staining, fever, or more than bearable local discomfort.

In a series of 21 infants aged 3 to 27 months suffering from anaemia with a low colour index specimens of bone marrow taken from the iliac crests before and after treatment showed an increase in the proportion of sideroblasts from less than 2% to between 6 and 46% of all nucleated cells of the erythrocyte series. The haemoglobin level rose by 1·5% daily, with obvious clinical improvement. The average haemoglobin level was 54·5% (100%=14·8 g. per 100 ml.) initially, and rose in 2 weeks to an average of 75·1% and in 10 weeks to 87%. The average dose of imferon was 5 injections of 1 ml. each, the total dose varying from 150 to 500 mg. Fe. There were no controls. The effect of imferon on the anaemia of prematurity was studied in 14 infants aged 2 to 15 months, estimations of the haemoglobin level only being made. The average level initially was 49·3% (range 40 to 56%), 2 weeks after treatment 69·6%, and 10 weeks after treatment 77·5% (range 74 to 80%). This encouraged the authors to undertake a prophylactic trial of imferon in which 10 infants of birth weight 3 lb. 14 oz. to 4 lb. 13 oz. (1,760 to 2,180 g.) were given imferon and their haematological progress compared with that of 10 control subjects of birth weight 3 lb. 2 oz. to 4 lb. 7 oz. (1,420 to 2,050 g.). Those in the former group whose birth weight was less than 4 lb. (1,830 g.) were given 250 mg. Fe and those between 4 and 5 lb. (1,830 and 2,270 g.) 150 mg. during the third week of life. Bone-marrow smears showed that sideroblasts, which were absent before treatment, constituted 6 to 10% of the nucleated cells afterwards. The initial fall in haemoglobin level was less and the level at 16 weeks (average 79·7%) was consistently higher in the treated group than in the control group (average 67·1%). A further 10 cases of anaemia associated with various surgical conditions were also treated with dramatic improvement.

The authors conclude that the intramuscular injection of imferon is followed by a rapid clinical and haematological response, which is maintained for many months. Infection prevents the utilization of iron whether given by the parenteral or by the oral route, but in its absence the treatment even of out-patients by daily or weekly injections of imferon is successful. The indications for its use are intolerance or resistance to oral treatment. cases in which home conditions are bad and a speedy rise in haemoglobin level is required, to obviate blood transfusion, and in the prevention of the anaemia of prematurity. An equation is given for the calculation of dosage according to body weight and haemoglobin level.

A. White Franklin

1024. Staphylococcal Pneumonia and Empyema in Infancy

W. E. Bloomer, S. Giammona, G. E. Lindskog, and R. E. Cooke. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **30**, 265–274, Sept., 1955. 3 figs., 26 refs.

The incidence of primary staphylococcal pneumonia in infants has increased since the introduction of antibiotics. The infection may be fulminating and rapidly fatal, or it may lead to multiple pulmonary abscesses, empyema, tension pneumothorax, and later to residual bullous cysts. Between 1944 and 1955, 11 proved cases of staphylococcal pneumonia were seen at the New Haven Hospital, Connecticut. Most of the patients, who were between 1½ and 16 weeks of age, were admitted within 7 days of the onset of symptoms. Empyema was present in 9 and pneumothorax in 4. The organisms were sensitive to penicillin in only 3 cases, erythromycin and chloramphenicol proving the most effective antibiotics. Repeated thoracentesis was performed in one case and closed suction drainage in 8 cases. There were no deaths in the series and the average stay in hospital was 32 days.

The severity of the infection and the sudden onset of complications are emphasized. The authors state that drainage is preferable to repeated aspiration, and that antibiotics must be given for several weeks. Decortication of the lung is rarely necessary and lytic enzymes are not advised. Residual air cysts usually disappear in the course of a few months.

S. F. Stephenson

1025. Cerebral Palsy. A Practical Routine for Discerning Oculomotor Defects in Cerebral Palsied Children

G. P. Guibor. *Journal of Pediatrics* [*J. Pediat.*] **47**, 333–339, Sept., 1955. 5 figs., 10 refs.

Ocular defects exist in over 50% of patients with cerebral palsy resulting from central nervous system derangement. These ocular motor defects should be detected before degeneration of vision occurs in these children. Early treatment of these motor defects will develop vision and may improve general motor ability, especially in patients with athetosis or ataxia. Simple tests are therefore suggested for detecting the presence of strabismus by the corneal reflection test, conjugate defects by the motility test, and subnormal vision by the means of the "E" game. An "E" chart for 10 feet [3 metres] distance testing instead of 20 feet distance is presented. This "E" chart gives percentages of visual efficiency as well as ordinary visual notations. Other tests such as the near vision and fixation tests are purposely omitted in this paper.—[Author's summary.]

Medical Genetics

1026. **Variable Manifestations of Plasma Thromboplastin Component Deficiency**
B. RAMOT, B. ANGELOPOULOS, and K. SINGER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 80–88, July, 1955. 3 figs., 30 refs.

This study, from the Michael Reese Hospital, Chicago, is based upon three families various members of which showed a deficiency of the plasma thromboplastin component (P.T.C.), or Christmas factor. In the first family the asymptomatic mother of the severely ill male propositus showed decreased thromboplastin generation, although her prothrombin time was normal. In the second, 3 brothers exhibited only mild haemorrhagic manifestations, but tests showed that they all had decreased thromboplastin generation. In the third family the mother was found to have normal thromboplastin generation, although her son was severely afflicted. The thromboplastin generation test is a sensitive procedure which is of assistance in detecting the expressivity of an abnormal gene in mild cases and in some maternal conductors.

The authors remark upon the variable degree of P.T.C. deficiency in different families and the constancy of the syndrome within the same sibship, deducing that the abnormal gene requires activation by some other factor or factors, probably of a genetic nature. The clinical manifestations result from the interaction of the abnormal gene and its modifier. Such a genetic situation is comparable to the inheritance of the sickle-cell trait, wherein the quantity of abnormal haemoglobin S varies from 20 to 50% in heterozygous carriers as a group, but may be relatively constant in members of the same family.

The significance of modifying factors which determine the expressivity of an abnormal gene becomes apparent when quantitative estimation of the fundamental pathological change is possible. For this reason the thromboplastin generation test may be of considerable value in investigating cases showing the P.T.C.-deficiency syndrome. *A. J. Duggan*

1027. **The Mechanism of Inheritance of Multiple Cartilaginous Exostoses.** (Le mécanisme héréditaire des exostoses multiples cartilagineuses)
U. PFÄNDLER. *Journal de génétique humaine* [*J. Génét. hum.*] **4**, 164–180, Sept., 1955. 4 refs.

The work of Stocks and Barrington has shown that the condition of multiple cartilaginous exostoses is clearly determined by a dominant gene, but its inheritance shows certain features which have hitherto remained unexplained. These are the unexpectedly high proportion of individuals affected within any affected family group, the preponderance of males (60 to 70%) among affected individuals, and the fact that affected males have a higher proportion (52%) of affected offspring than do affected females (41%).

The present author has studied the 183 pedigrees of Stocks and Barrington, together with those of 2 affected families reported by Roeder and one personally investigated, and presents a statistical analysis of these data showing the proportions of affected males and females among the offspring of affected mothers and affected fathers, giving estimates of apparent sex differences in penetrance (male 91%, female 68%) and investigating the evidence for the existence of incomplete sex-linkage. Further statistical assessment gives results which are consistent with a hypothesis that the gene responsible for the trait augments the resistance of the gamete or zygote whether carried on the X or the Y chromosome, but more especially when carried on the latter. It is therefore suggested that the condition is controlled by a dominant gene and is partially sex-limited by the higher survival rate or greater vitality of Y-bearing gametes carrying the gene responsible. *R. H. Cawley*

1028. **On the Inheritance of Muscular Dystrophy**
J. N. WALTON. *Annals of Human Genetics* [*Ann. hum. Genet.*] **20**, 1–13, Aug., 1955. 17 refs.

By means of a detailed survey of the records of hospitals and the circularization of general practitioners in the counties of Northumberland and Durham, the author obtained information about 102 cases of muscular dystrophy. This was believed to approach complete ascertainment of such cases in the area, so that the incidence is estimated as approximately 1 in 22,000 of the general population. The author examined 84 patients personally on at least 2 occasions, and in most of these cases muscle biopsy was performed. All available parents and sibs were examined. Of the 18 patients who were not examined, 11 were dead.

Out of 56 patients with the Duchenne (" pseudohypertrophic ") type, occurring in 41 sibships of 34 families, 45 were examined. In 20 families there was an isolated case, 8 families had more than one affected male in the same sibship, and in 6 families more than one fraternity was affected. The distribution clearly supports the hypothesis of sex-linked recessive inheritance; there is in addition evidence of a high mutation rate, estimated as approximately $4{\cdot}3 \times 10^{-5}$ (Haldane method).

The natural history and mode of inheritance of facioscapulo-humeral muscular dystrophy appeared to differ from those of the limb-girdle type. There were 22 affected and 23 unaffected individuals in 4 families, and the evidence obtained supports the hypothesis of transmission by an autosomal dominant gene, possibly in some circumstances sex-limited or incompletely manifested.

The limb-girdle type of muscular dystrophy appears to be intermediate between the above types in its rate of progress. In only 2 of the 18 families having affected members was more than one person affected in any

generation. In only one family were previous generations involved. The evidence here is consistent with transmission by an autosomal recessive gene; one family showed an atypical distribution.

(A note by Race on the blood groups of affected individuals and some of their sibs and parents discloses no evidence of linkage. The demonstration of extramarital children in one affected family provides ancillary evidence for a sex-linked recessive gene controlling the Duchenne type, and in another for the action of an autosomal gene with a dominant effect in the facioscapulo-humeral type.)

(A further note by Philip on colour vision and linkage studies reports the demonstration of crossing-over between genes concerned in red blindness and the Duchenne type of dystrophy.) *R. H. Cawley*

1029. **Report of a Family Suffering from Friedreich's Disease, Peroneal Muscular Atrophy, and Schizophrenia**
M. SHEPHERD. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 297–304, Nov., 1955. 22 refs.

1030. **The Mechanism of Inheritance of Dupuytren's Contracture.** (Le mécanisme héréditaire de la maladie de Dupuytren)
U. PFÄNDLER. *Acta geneticae medicae et Gemellologiae* [*Acta Genet. med.* (*Roma*)] **4**, 296–319, Sept., 1955. Bibliography.

The author analyses 24 families which show particularly strongly the influence of heredity on Dupuytren's contracture, selected from amongst those reported in the literature. The genealogies of these families show single-factor dominant inheritance with variable penetrance—and especially transmission by apparently unaffected females. Altogether, the affected sibships include 90 affected males out of 178 (from which a penetrance of 93·6% is calculated), but only 17 affected females out of 113 (penetrance 42·9%). Unaffected sibships in the same genealogies contain 38 males and 43 females, a sex ratio which does not differ significantly from the normal.

Calculations suggest that the deficit of affected females cannot be explained by partial sex-linkage or by autosomal dominance. The theory is therefore advanced that the responsible gene is lethal for 60% of XX zygotes, and that affected maternal gametes are selectively fertilized by Y spermatozoa. The theoretical proportions of affected and normal subjects calculated on this basis tally well with those observed. *G. C. R. Morris*

1031. **Infantile Hypertrophic Pyloric Stenosis: Data on 81 Pairs of Twins.** [In English]
B. MACMAHON and T. MCKEOWN. *Acta geneticae medicae et Gemellologiae* [*Acta Genet. med.* (*Roma*)] **4**, 320–329, Sept., 1955. 17 refs.

Among 3,982 cases of infantile hypertrophic pyloric stenosis treated at hospitals in Birmingham, Liverpool, Manchester, Newcastle upon Tyne, and Sheffield during periods ranging from 4 to 23 years, 87 occurred in twins—an incidence nearly equal to that of twins in general. In 6 cases both twins were affected, the incidence of the condition in the partners of affected twins thus being nearly 9% (compared with 0·3% in all births, and 5·8% among sibs born subsequently). Although the data were insufficient for determination of the type of twinning in most cases, in 65 pairs the sex distribution was known. Of the 39 like-sexed pairs, 18 might have been expected to be monozygous, but only 4 were concordant in respect of pyloric stenosis. Of the 26 unlike-sexed pairs, 2 were concordant. None of the 8 female pairs was concordant. *G. C. R. Morris*

1032. **Phenotypes and Genotypes in Cystinuria**
H. HARRIS, U. MITTWOCH, E. B. ROBSON, and F. L. WARREN. *Annals of Human Genetics* [*Ann. hum. Genet.*] **20**, 57–91, Aug., 1955. 7 figs., 5 refs.

In a previous paper (Harris and Warren, *Ann. Eugen.* (*Camb.*), 1953, **18**, 125) the authors have drawn attention to two types of family affected with cystinuria—those showing sharp segregation into two classes of individual with grossly increased and with normal cystine excretion respectively ("recessive cystinuria"); and those with, in addition, a third type of individual in whom cystine excretion is moderately increased ("incompletely recessive cystinuria"). The familial incidence suggests that in families of the first type the abnormal individuals are homozygous for a rare recessive gene; and that in families of the second type the two abnormal phenotypes are respectively homozygous and heterozygou for a rare mutant gene.

A more extensive biochemical investigation has now been performed at the London Hospital and the Galton Laboratory, University College, London, by the quantitative estimation of cystine (by polarography) and lysine and arginine (by microbiological determination) and the qualitative estimation of ornithine (by ionophoresis) in the urine of propositi presenting with cystine stone formation and of their parents and sibs. Of the 26 abnormal individuals tested from 19 families showing recessive cystinuria, all had a grossly increased output of cystine, lysine, and arginine, whereas the 25 normal individuals tested all gave values within normal limits. The familial configuration is what would be expected on the hypothesis that affected individuals are homozygous for a rare recessive gene.

In the 8 families showing incompletely recessive cystinuria 3 phenotypes were characterized as showing (1) grossly increased cystine, lysine, and arginine excretion, with excretion of large amounts of ornithine; (2) moderately increased cystine and lysine excretion, the output of arginine and probably of ornithine being normal; and (3) values within the normal range for all four amino-acids. The familial distribution is consistent with the hypothesis that the first phenotype is determined by the homozygous state for a rare gene and the second by the heterozygous state.

It is not at present possible to distinguish biochemically or clinically between homozygotes for recessive cystinuria and homozygotes for incompletely recessive cystinuria; and it is not clear from evidence yet available whether the two genes are allelomorphic or at different loci.
R. H. Cawley

Public Health

1033. Changes in Body Weight Associated with Age and Marital Status

C. R. Lowe and J. R. Gibson. *British Medical Journal* [*Brit. med. J.*] **2**, 1006–1008, Oct. 22, 1955. 5 figs., 10 refs.

The authors have analysed data concerning age, height, weight, marital status, and, in the case of women, the number of children, obtained from records made at the pre-employment medical examination of 1,684 men and 5,081 women on entry to two large industrial firms in Birmingham during the last 10 years. The mean weight of the women increased fairly regularly by about 3 lb. (1·4 kg.) for every 5 years of age, rising from 123·8 lb. (56·1 kg.) in the age group 20–24 to 139 lb. (63 kg.) at age 45–49, an increase of a little over 15 lb. (6·8 kg.) in 25 years; at higher ages there was no further increase. These findings are in agreement with similar observations made in 1926 and in 1943. The mean weight of the men, however, varied little with age, and in none of the 5-year age groups between 20–24 and 45–49 did the mean weight deviate by more than 1 lb. (0·45 kg.) from the figure of 149·1 lb. (67·6 kg.), the mean for the whole series. The authors point out that these findings differ from Galton's observations made in 1884, and from Cathcart's for the years 1929–32, who found increases in weight among men comparable to those here found in women; they do, however, agree with data collected by the Ministry of Food in 1943 and by the Ministry of Labour and National Service between 1939 and 1946. The authors are careful to emphasize that all these findings refer to a cross-section at a given time, and not to a follow-up of the same men at different ages.

In regard to marital status it was found that in each 5-year age group married women were heavier than single women, the difference increasing fairly regularly with age. Between the age groups 20–24 and 45–49 the weight of married women increased by more than 16 lb. (7·3 kg.), whereas the weight of single women increased by less than 6 lb. (2·7 kg.); but child-bearing is not the sole or even the most important reason for this difference, for in each age group married women without children were heavier than single women. There was no significant difference between the weights of single and married men.

F. T. H. Wood

1034. Diverging Sex-morbidity Trends in Cancer of the Mouth. A Hospital Morbidity Study

M. H. Russell. *British Medical Journal* [*Brit. Med. J.*] **2**, 823–827, Oct. 1, 1955. 1 fig., 15 refs.

The author has investigated the morbidity rates for cancer of the mouth in each sex based on "new" cases sent for treatment at the Christie Hospital and Holt Radium Institute, Manchester, and its peripheral clinics in the region, covering a population of approximately 3,500,000, for the two periods 1935–9 and 1945–9. For purposes of classification the cases were divided into three groups according to site: (1) tongue, (2) the main oral cavity, and (3) the faucial region (or posterior oral cavity).

The total number of new patients for the first period was 1,077 males and 119 females, and for the second period 777 males and 209 females, representing a decrease of 28% for men and a corresponding increase of 76% for women. When the figures according to site were considered separately, the most striking change was the 60% increase in cancer of the tongue in females, while the greatest decrease in males was 50% in the faucial region. The over-all incidence of cancer of the mouth still remains low until the 6th decade of life. The reduction in the morbidity rate in males has occurred in varying degrees in all age groups, whereas the increase in cancer of the tongue in females is apparent at younger ages, although it reaches its peak at age 75 and over.

When the differential rates in urban and rural areas were considered, it was found that the most striking decrease for men (50%) was in county boroughs. In the same areas the female rate has increased by 46%. From these figures the author concludes that residence in the most urbanized communities results in intensification of certain aetiological hazards for both sexes, but that meanwhile some other factor not solely related to residence in urban areas has become less potent for men and more potent for women. A recent hypothesis regarding the aetiology of carcinoma is that it is due to local aggravation in men but to a systemic factor in women. The author suggests, in view of this, that one line of investigation might be the investigation of microcytic anaemia in women in this area.

Elaine M. Osborne

1035. Mortality among Workers in Cigarette Factories

H. F. Dorn and W. S. Baum. *Industrial Medicine and Surgery* [*Industr. Med. Surg.*] **24**, 239–241, June, 1955 [received Sept., 1955]. 4 refs.

Information about the number of deaths and the causes of death among employees of a large American firm engaged in the manufacture of tobacco products, all of whom are covered by a comprehensive insurance scheme, has been analysed for the period October, 1946, to December, 1952; the number of person-years of observation among those employed in cigarette manufacture was 70,532. Study of these data does not suggest that any cause of death is disproportionately common among workers engaged in processing cigarettes as compared with those otherwise employed. Compared with that among the general population of the two States where most of the employees work the mortality among the cigarette workers from all causes, from cancer, and from cardiovascular diseases was distinctly low; in

respect of respiratory cancer and coronary arterial disease the differences were inappreciable.

No evidence was obtained that the apparently lower mortality among the cigarette workers was attributable to a rapid labour turnover or to removal of seriously ill employees from the pay-roll. *Richard Doll*

1036. **Deaths from Scarlet Fever in the Twentieth Century**

H. PAUL. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] 46, 363–367, Sept., 1955. 1 ref.

Since its recognition as a specific disease in the 16th and 17th centuries, scarlet fever has undergone a number of changes in severity, though the author points out that, in general, the important changes have been in the fatality rather than in the incidence of the disease. At the beginning of the 20th century the death rate from scarlet fever was about 110 per million in England and Wales (it had been 720 per million in 1870), 40 per million in the U.S.A., and 300 to 400 per million in Germany. Since then the mortality has fallen steadily in most countries for which records are available, particularly since sulphonamides were introduced. Germany is a notable exception, no substantial fall in mortality from scarlet fever having occurred until 1946. The author stresses, however, that for comparison to be valid all streptococcal infections should be included and scarlet fever not considered alone.

The changes in the incidence of and mortality from scarlet fever which have taken place since 1939 in various countries are compared. Incidence has fallen materially in Canada, the U.S.A., and Australia, but not in England and Wales, South Africa, or New Zealand. Mortality has also fallen markedly, but still remains relatively high in Canada; in most of the countries named the mortality from scarlet fever today is relatively trivial.

The author concludes with a comment on the decline in hospital treatment of this disease and the futility of isolation when the carrier rate may be as high as 1 in 3. *R. J. Matthews*

1037. **The Relation between the Fluorine Content of Drinking Water, Fluorosis, and Dental Caries.** (О взаимосвязи между содержанием флора в воде, флюорозом и кариесом)

V. A. KNIZHNIKOV. *Гигиена и Санитария* [*Gigiena*] 13–17, No. 10, Oct., 1955. 4 figs., 10 refs.

The author has investigated the relation, if any, between the fluorine content of the local water supply and the presence of fluorosis or dental caries among the population of three localities in central Kasakhstan, where a total of 2,202 persons, mainly school-children, were examined. The fluorine concentration in the drinking water in the three areas varied from 0 to 6 mg. per litre. No direct relationship could be found between fluorine concentration and the presence or degree of fluorosis. It was thought that the toxic action of fluorine may have been reduced by the presence in the water of considerable quantities of calcium and iodine. In some cases a severe degree of fluorosis was found to co-exist with a high incidence of caries; on the other hand persons in the initial stages of fluorosis, that is, with isolated small chalky spots on the dental enamel, exhibited a very low incidence of caries. *A. Swan*

1038. **Control of Wound Infection in a Thoracic Surgery Unit**

R. BLOWERS, G. A. MASON, K. R. WALLACE, and M. WALTON. *Lancet* [*Lancet*] 2, 786–794, Oct. 15, 1955. 4 figs., 23 refs.

A thoracic unit at Poole Hospital, Nunthorpe, Middlesbrough, which started work in 1942 had to be temporarily closed on account of a considerable increase in the incidence of wound infections, which amounted to 10·9% in the first 5 months of 1952. The interval between operation and the appearance of clinical signs of infection was at first often as long as 3 weeks, but became progressively shorter and by 1952 it was rarely more than 2 or 3 days. The infection was due in most cases to *Staphylococcus aureus*. The authors describe the detailed investigations which were made to discover the source of infection and discuss the possibility that the staphylococci may have become resistant to penicillin or have increased their virulence. Staphylococci were found in the air and dust not only in the wards and corridors, but also in the operating theatre. After correction of faults of procedure, improvement of the ventilation, and various measures such as exclusion of blankets from the theatre, avoidance of unnecessary movements of the staff, and discard by the surgeons of punctured gloves a marked reduction in the incidence of infection was obtained. The authors are of the opinion that strict asepsis is more rewarding in the prevention of wound infection than the liberal use of antibiotics. *Franz Heimann*

EPIDEMIOLOGY AND IMMUNIZATION

1039. **Improvement of the Quality of Diphtheria Immunization.** (Улучшить качество прививок против дифтерии)

N. M. RYBKINA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 3-7, No. 9, Sept., 1955. 2 figs.

[The real purpose of this paper from the Central Public Health Administration of the Ministry of Health, Moscow, is to deliver an official exhortation to Russian bacteriologists and paediatricians to improve the quality of immunization against diphtheria. However, a number of epidemiological data of general interest are given.]

From 55 to 65% of all cases of clinical diphtheria in the U.S.S.R. occur in children between the ages of 1 and 6 years, while cases in school-children (7 to 14 years) account for 10·3 to 18·9%. As in western countries, the incidence of diphtheria among adults has been increasing during recent years, particularly in the larger cities in which up to 95% of the child population is immunized. In Leningrad the proportion of cases occurring in patients over 15 years was 38·9% in 1952 and 40·3% in 1953, and in Moscow the corresponding figures were 33·1% and 29%. Case fatality rates in the various parts of the country differed. In 1952 and 1953

the figures for Moscow were 0·5% and 0·4%, for Byelorussia 4·3% and 3·8%, and for the Ukraine 5·9% and 7%. The figures were considerably greater in outlying districts in some republics, reaching 13% in parts of the Ukraine and 18·4% in Kasakhstan. In the U.S.S.R. as a whole approximately 80% of fatal cases occurred in children under 6 years of age.

In certain areas the incidence of clinical diphtheria among the immunized is 5·4 to 7 times lower than among the non-immunized. On the other hand the proportion of immunized children among those developing clinical diphtheria is increasing, and had reached 80% in Leningrad and Moscow during 1952. In Kharkov the corresponding figures for children up to 12 years were 34% in 1946, 41·5% in 1948, 66% in 1950, and 64·6% in 1952. This spectacular increase in the incidence of diphtheria among the immunized may perhaps be related to the comparatively high proportion of Schick-positive children among the fully immunized. For instance, work carried out at the Kiev Epidemiological Institute showed that in only 37% of cases of diphtheria was the patient fully immunized, while field investigations in the same region showed that 24·6% of immunized children aged 1 to 9 were Schick-positive. Such findings necessarily cast doubt on the quality of the immunization procedure. A suggestion that the positive Schick reaction may be induced in immunized children by the repeated occurrence of other febrile infections is supported by the findings of Staroverova, who found that whereas only 5·2% of immunized children who had not subsequently suffered from febrile infections were Schick-positive, among those who had had 7 or more febrile infections since being immunized the proportion was 42·7%.

K. Zinnemann

1040. **Smallpox in France in 1955. Epidemiology and Prophylaxis.** (La variole en France en 1955. Epidémiologie et prophylaxie)
B. Le Bourdellès, M. Berger, M. Rodallec, M. Viguié, and R. Bellec. *Presse médicale* [*Presse méd.*] 63, 1247–1248, Sept. 24, 1955. 9 refs.

Nearly 100 cases of smallpox were diagnosed in France in 1955, with 20 deaths—the most important epidemic of this disease that has occurred there for 30 years. The epidemic originated from a soldier who had been repatriated by air from Indo-China because of pulmonary tuberculosis. He was permitted to stay with his family in Vannes, Brittany, for the 5 days November 19–24, 1954, and his son, an infant of 11 months, was admitted to hospital on December 9 with a diagnosis of "pemphigus". Several contacts of this child in the hospital developed smallpox, the diagnosis being confirmed by laboratory tests on January 5, 1955. This first focus of infection gave rise to 74 cases, with 16 deaths, between January and March, all being centred around the hospital, the victims including patients, hospital staff visitors, and contacts in the district. A second focus of infection was set up in a hospital in Brest in April by the transfer of a patient from Vannes after an apparently adequate period of isolation and careful disinfection, the patient developing smallpox the day after her arrival. This new outbreak was responsible for 21 definite cases with 4 deaths. In addition, there were 11 cases of febrile illness without a rash in incompletely immunized persons, which were probably *formes frustes*—cases of non-eruptive smallpox.

The story of this epidemic underlines most of the errors of management so often made in connexion with smallpox importations into western countries. The diagnosis of the first cases was made difficult by the "polymorphism" shown by the disease, with abortive and non-eruptive forms, in a partially immunized community. The extreme infectivity of the type of variola major imported from the Far East and the vulnerability of countries with frequent Far Eastern air connexions were once again demonstrated. The comparatively large number of cases contracted in hospital draws attention to the necessity of providing, and maintaining at all times, facilities for the complete isolation of suspected cases of smallpox, so that they will not have to be treated, as in this outbreak, in hospital wards containing general medical patients, and of the regular vaccination of medical and nursing staff. Immediately a case of smallpox is diagnosed the infection should be localized not only by complete isolation of the affected patient, but by the tracing of all contacts and their surveillance for 16 days, as well as by vaccination. Mass vaccination may sometimes become necessary when the vaccination state of the population is low, but the need should be reduced to a minimum in France by the regular application of measures provided by the law for the vaccination of the public.

A trial was made during this outbreak of the effect of prophylactic injections of gamma globulin in a dosage of 0·2 ml. per kg. body weight on subjects in whom vaccination was contraindicated and on unvaccinated persons who had been exposed to infection and who were vaccinated presumably during the incubation period. This measure appeared to have a favourable effect in children, either providing total protection or producing attenuation of the disease. *H. Stanley Banks*

1041. **Epidemiology of Influenza. Comparative Serological Observations in England and the United States**
F. M. Davenport, A. V. Hennessy, C. H. Stuart-Harris, and T. Francis. *Lancet* [*Lancet*] **2**, 469–474, Sept. 3, 1955. 5 figs., 14 refs.

In this joint study carried out at the Universities of Michigan and Sheffield the haemagglutination-inhibiting titres to various strains of influenza A, A-prime, and swine influenza virus of sera from large samples of the populations of Sheffield, England (1,650 persons), and Ann Arbor, U.S.A. (1,800 persons) were compared. Aliquots of sera were pooled by two-year age intervals from the first year of life up to and including the 69th year, each pool being composed in most cases of samples of serum from 50 persons.

In the sera from both countries the composite antibody levels varied according to age, as was to be expected from previous studies, and reflected the past exposure of the respective populations to the various antigenic types of virus prevalent at different periods. While the anti-

body levels to the swine influenza virus, which is widely thought to have been the antigenic type prevalent during the 1918 influenza pandemic, were similar in the two countries, the antibodies to influenza-A strains and, to a lesser extent, the A-prime strains, were lower in the Sheffield than in the Ann Arbor population. The former strains were prevalent in the 1930s and the latter became prevalent from 1946 onwards. The lower antibody levels found against these strains in the Sheffield sample are considered to be of help in explaining the higher mortality from influenza which has been observed in Great Britain since 1932. *J. E. M. Whitehead*

1042. **Influenza Virus C Infection in England**
B. E. ANDREWS and J. C. MCDONALD. *British Medical Journal* [*Brit. med. J.*] **2**, 992–994, Oct. 22, 1955. 1 fig., 13 refs.

Workers in the U.S.A. have isolated influenza virus C from throat washings of patients with mild clinical influenza and have also found serological evidence of infection. Study of the age distribution of both haem-agglutination-inhibiting and complement-fixing antibodies has indicated that infection occurs widely in childhood, with the result that many adults possess demonstrable levels of antibody. In this and the following paper [see Abstract 1043] similar findings are reported in Great Britain. At the Virus Reference Laboratory, Colindale, between 1953 and 1955 serological evidence of virus-C infection was found in 10 cases. In one case the virus was isolated from a throat swab from a 2-year-old girl who was suffering from a febrile cold and cough; her sister, who had a cold on the same day, later showed a high antibody titre to influenza virus C. Serological evidence of infection was found in 2 adults with mild influenza-like illnesses and in 6 other adults at routine blood examination, 5 of whom had colds in the interval between two blood examinations. The age distribution of complement-fixing antibody was studied in specimens of serum from different parts of the country; it was found that the proportion of specimens in which the titre was 1 in 10 or higher rose from 5% in children under 4 years to 61% in patients aged 25 to 34.
J. E. M. Whitehead

1043. **Influenza A and C in Glasgow, 1954**
N. R. GRIST. *British Medical Journal* [*Brit. med. J.*] **2**, 994–997, Oct. 22, 1955. 9 refs.

Serological examination for evidence of influenza virus infection was carried out in all adults and infants admitted to pneumonia wards in Ruchill Hospital, Glasgow, between October, 1953, and July, 1954. In 93 infants no evidence that infection with influenza virus C was the cause of the illness for which they were admitted to hospital was found, although in 3 there were haem-agglutination-inhibiting (H.I.) titres of 1 in 64 or higher, but no detectable complement-fixing (C.F.) antibody titres. A rising titre against influenza virus A was found by both methods in 2 infants with cough and fever. Of 199 adults there was serological evidence of influenza virus-C infection in 7 and of influenza virus-A infection in 10. The clinical diagnoses in these adults were diverse. Since the serological diagnosis was reached in retrospect no information was available concerning influenzal prodromes to the illnesses. In the C.F. test for influenza virus C 14% of specimens of adult serum gave titres of 1 in 16 or higher, and in the H.I. test 36% gave titres of 1 in 32 or more. There was a positive correlation between the results by the two tests, although some scatter was observed. The age distribution of antibody titres was in line with that observed by Andrews and McDonald [see Abstract 1042]. It is pointed out, however, that the 7 cases of influenza virus-C infection in the present series occurred in adults aged 45 to 69 years and not in children. *J. E. M. Whitehead*

1044. **The Control of Tuberculosis—House to House Spread of Disease: Further Observations**
B. BENJAMIN, R. GRENVILLE-MATHERS, and H. J. TRENCHARD. *Tubercle* [*Tubercle* (*Lond.*)] **36**, 307–309, Oct., 1955. 6 refs.

In continuation of an earlier study carried out on new housing estates near London (Grenville-Mathers *et al.*, *Tubercle*, 1954, **35**, 294; *Abstracts of World Medicine*, 1955, **18**, 165) an attempt was made in the present study by the use of statistical methods to assess the incidence of tuberculosis in neighbouring houses, the notification figures for five areas with a total population of about 640,000 being analysed.

It was found that the chance of tuberculosis occurring in adjacent houses was significantly greater than expected in Hendon, Luton, and Northampton, greater (not significantly) in Harrow, and less (not significantly) in Bedford. A study of selected groups within these areas showed that persons working in the same factories tended to live next door to or near each other. It is considered that the spread of tuberculous infection from house to house purely as a result of geographical propinquity is not therefore likely to be the only factor explaining the non-random distribution of notifications of tuberculosis in certain areas. *John Lorber*

1045. **The Epidemiology of Poliomyelitis: Epidemic Years in Austria and Switzerland.** (Zur Epidemiologie der Poliomyelitis: Epidemiejahre in Österreich und der Schweiz)
W. DONLE. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] **11**, 161–187, 1955. 5 figs., bibliography.

With the help of charts the author relates the incidence of poliomyelitis to the weather experienced in Austria and Switzerland during the period 1931–7 and in the epidemic years 1941 and 1947. He points out that the occurrence of an epidemic in each of the years 1931, 1936, 1937, 1941, and 1947 was associated with the occurrence of a long and relatively uninterrupted period of hot weather beginning in May, the incidence of poliomyelitis reaching its maximum in July and August. The number of cases occurring was directly proportional to the number of hot days during June, July, and August. With the onset of periods of cold weather the incidence of poliomyelitis showed a decline.
Franz Heimann

Industrial Medicine

1046. The Incidence and Special Features of Cancer of the Lung in Asbestosis. (Über Häufigkeit und Besonderheiten des Lungenkrebses bei Asbestose)
G. JACOB and H. BOHLIG. *Archiv für Gewerbepathologie und Geweberhygiene* [*Arch. Gewerbepath. Gewerbehyg.*] **14**, 10–28, 1955. 4 figs., bibliography.

In both parts of Germany cancer of the lung occurring in asbestos workers is recognized as an industrial disease, and it has been inaccurately reported that the incidence of the disease is high among workers exposed to asbestos dust. It is remarkable, however, that the occurrence of lung cancer in asbestos workers has been frequently reported only from Germany and Great Britain. From the U.S.A. and France such reports have been very few, while from the U.S.S.R., Finland, Italy, and South Africa there have been no reports at all. In Canada, where some 3,200 asbestos workers are employed, no cases of asbestosis with lung cancer are on record.

At the City Hospital, Dresden, the authors have studied 343 cases of asbestosis from the Dresden area, where some 2,000 asbestos workers are employed, of whom probably only 1 in 4 is actually exposed to harmful concentrations of dust. In 15 of these 343 cases there was associated active tuberculosis, and 4 others had developed cancer of the lung. The case history of each of these 4 is given in detail. On account of the changing population and of the very long latent period in the growth of such tumours the incidence of cancer in asbestosis is extremely difficult to assess. During the last 20 years the average number of asbestos workers throughout Germany has varied between 3,000 and 4,000. The literature has been searched, and is here freely quoted, in an attempt to ascertain the expectation of cancer of the lung from any cause in such a population, and it is calculated that of any group of 4,000 persons between 2 and 16 may be expected to develop cancer of the lungs. During these 20 years only 13 cases of respiratory cancer in asbestos workers have been reported in the whole of Germany and these include 3 cases of cancer of the pleura and peritoneum. To these must now be added the 4 cases from Dresden, giving a total of 17. Even if only half the cases occurring were discovered the incidence would not be outstanding as compared with that of lung cancer in the general population.

The peculiarities of lung cancer in asbestos workers are discussed. The age incidence reaches a peak in the early fifties. The duration of exposure to asbestos dust in published cases has varied between 19 months and 42 years, the latent period between the start of the exposure and the manifestation of lung cancer averaging 22 years. The site is most often in the upper lobe, and histological examination of the tumour frequently shows squamous epithelium. These characteristics are examined and some are found to be variable.

M. A. Dobbin Crawford

1047. Industrial Lead Poisoning in Relation to Climate
D. O. SHIELS. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **4**, 178–182, Aug., 1955. 1 fig., 2 refs.

A comparison of the incidence of lead poisoning at three widely separated places in Australia, namely, Mount Isa in Queensland, Port Pirie in South Australia, and Melbourne, Victoria, which have climates varying from hot and dry to temperate, revealed that persons excreting 0·3 mg. (or more) of lead per litre of urine were more likely to show overt signs and symptoms of lead poisoning where the climate was hot.

The author therefore reviewed 234 cases of industrial lead poisoning which occurred in Melbourne over 16 years, and found that the incidence of cases requiring removal from the lead hazard was much greater in the cold months of the year (June, July, and August) than in the hot months (December, January, and February). It was considered that factors such as length of service, individual idiosyncrasy, and nature of the lead compound being handled would not exert an influence likely to produce this result. Moreover, determination under varying conditions of the concentration of lead in the air at the various places of work failed to shown any correlation between this value and the seasonal temperature. Nor could any evidence be found of increased production in the lead industries in Melbourne during the cool months, this figure remaining about the same throughout the year. It is suggested that in summer increased consumption of fresh fruit, containing sodium citrate, and citric, malic, and similar acids, may increase the urinary excretion of lead. This factor might operate in Melbourne, but would not be of significance at Mount Isa where fresh fruit and vegetables are scarce owing to the arid climate. Another possible factor may be the increased elimination of lead in the sweat in the hotter months. Thus for any given concentration of lead in the urine, the total amount of lead eliminated from the body would be greater in conditions producing much loss of sweat; hence in the hot climate of Mount Isa the mobilization of lead in the body would be greater than at Melbourne, and the possibility of the overt manifestation of lead poisoning would thus be enhanced.

[It should be noted that the review of cases in Melbourne was not confined to those excreting 0·3 mg. or more of lead per litre of urine, so that these cases were not selected in the same way as those at the other centres. This is not indicated, and the apparent anomaly between the incidences at Mount Isa, Port Pirie, and Melbourne and the variation in incidence throughout the year in Melbourne are not discussed. *W. K. S. Moore*

1048. Tolerance of Men to Work in Hot, Saturated Environments with Reference to Mines Rescue Operations
A. R. LIND, R. F. HELLON, J. S. WEINER, and R. M. JONES. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **12**, 296–303, Oct., 1955. 5 figs., 17 refs.

Anaesthetics

1049. **The Mechanism of Increased Intracranial Pressure Induced by Morphine**

A. S. KEATS and J. C. MITHOEFER. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 1110–1113, June 30, 1955. 3 figs., 15 refs.

It has long been known that morphine causes a rise in cerebrospinal fluid (C.S.F.) pressure, and in the present authors' view the rise is secondary to an increase in arterial carbon dioxide tension, brought about by decreased ventilation.

In 19 patients in whom spinal analgesia had been induced by means of a catheter the C.S.F. pressure was determined after operation. Some patients were given morphine alone, some morphine and nalorphine, and some nalorphine alone. When morphine or nalorphine was given alone there was an increase in the C.S.F. pressure, but previous administration of nalorphine lessened the rise due to morphine. Voluntary hyperventilation produced a fall in the C.S.F. pressure in 3 patients, while in 2, in whom alveolar carbon dioxide tension was measured at different rates of ventilation, a fall in this value was followed by a fall in the C.S.F. pressure.

Ronald Woolmer

1050. **Adhesive Arachnoiditis and Vascular Blockage Caused by Detergents and Other Chemical Irritants: an Experimental Study**

E. W. HURST. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **70**, 167–178, 1955. 10 figs., 14 refs.

Contamination of analgesic agents by detergents has recently been blamed for the neuropathy which sometimes complicates spinal analgesia. The present author has attempted to trace the effect of the introduction into the cerebrospinal fluid (C.S.F.) of monkeys of a number of chemical substances, including quaternary ammonium compounds, some of them cationic detergents, an anionic detergent, a non-ionic detergent, phenol, and horse serum. When these substances were introduced into the C.S.F. in appropriate concentration the following lesions were observed: (1) peripheral degeneration of the spinal cord, degeneration of some nerve roots, and ascending degeneration of posterior nerve roots; (2) cellular proliferation and inflammatory exudate in the meninges; (3) necrosis of the media and of the adventitia of the meningeal vessels, progressing to obliteration of the lumen and restriction of the blood supply to nervous tissue.

The author states that these lesions have also been observed in the human subject following spinal analgesia, and contamination of the analgesic agent with detergents has been blamed, regardless of the fact that clinically similar accidents occurred before detergents came into common use. He therefore suggests that a reappraisal is urgently needed of the toxic effects of analgesic agents themselves on the spinal cord of the experimental animal.

B. L. Finer

1051. **Hypothermia in Surgery. Analysis of 100 Clinical Cases**

H. SWAN, R. W. VIRTUE, S. G. BLOUNT, and L. T. KIRCHER. *Annals of Surgery* [*Ann. Surg.*] **142**, 382–400, Sept., 1955. 4 figs., 4 refs.

In this paper from the University of Colorado School of Medicine, Denver, the authors discuss the lessons learned from the application of a hypothermic technique of anaesthesia in 100 cases, 80 of them for operations for the repair of cardiac defects. Hypothermia was chosen primarily because it prolongs the time of tolerance of organs and tissues to ischaemia and thus makes possible the repair of cardiac defects under direct vision with circulatory arrest. It also reduces the operative risk by improving oxygenation and slowing the heart rate in cyanotic patients, especially children. It had been hoped that the accompanying hypotension would facilitate surgery, but the high incidence of reactionary haemorrhage during the postoperative warming period was disappointing. The hypothermia itself produces anaesthesia, so that minimal amounts of anaesthetic drugs (in this series, ether) are necessary, and then only during the cooling process.

Hyperventilation was used throughout in a deliberate attempt to produce an alkalosis with a *p*H of at least 7·5, which enables the myocardium to remain in potassium balance. Earlier animal studies had indicated that cardiac irritability during hypothermia was partly due to sympathetic–parasympathetic imbalance, vagal function being more depressed than sympathetic. To counter this, neostigmine was perfused into the base of the aorta immediately after it had been clamped; it was used in liberal doses as it can be antagonized readily by calcium. To the same end, atropine was not used in premedication. The cooling technique included complete immersion in ice-water, curarization as necessary to control shivering, and continuous rectal temperature recording and electrocardiography. The anaesthetic agent was discontinued once the temperature reached 31° C. (87·8° F.). Auricular fibrillation usually arises at 29° C. (84·2° F.) but is of no dangerous import. Temperatures down to 26° C. (78·8° F.) were commonly reached; below that there was an apparent rise in mortality, but this was partly due to the fact that the lowest temperatures were used in cases requiring the most complicated surgery and hence the longest period of occlusion.

In the series of 80 cases of operation on the heart there were 19 deaths, and in the remaining 20 cases 3 deaths. Mortality was significantly, though inexplicably, lower in females, but bore no relation to age. Ventricular fibrillation was the major complication met, more frequently in patients with hypertrophied hearts. When it occurred electrical defibrillation was used after an initial period of manual compression. On the minority of occasions when it was not successful by itself it was followed by coronary perfusion with potassium chloride solution and, if finally necessary to restore

tone to a very flabby heart, intracardiac injection of adrenaline. Meanwhile, if the stage of the operation allowed, the patient was warmed as rapidly as possible by intermittent short-wave diathermy applied to a well-insulated coil around the lower part of the body. The risk of burns with this technique and the need for an improved method of rapid warming (when it is impracticable to immerse the patient in warm water) are emphasized. Quinidine was not used as a routine, and digitalis only in patients in frank failure before operation. Of the 15 patients who had this complication, 10 were resuscitated, but only 3 eventually survived whereas of 7 patients who had cardiac standstill, 6 are still alive.

There were 4 deaths from postoperative haemorrhage, and the difficulty of differentiating shock from heart failure in the unfamiliar setting of the post-hypothermia period is emphasized. It is urged that haemostasis must be complete, and to that end the warming process should be almost complete before the chest is closed.

Donald V. Bateman

1052. **A Comparison of the Physiological Effects of Hypercapnia and Hypoxia in the Production of Cardiac Arrest**

G. H. A. Clowes, A. L. Hopkins, and F. A. Simeone. *Annals of Surgery* [*Ann. Surg.*] **142**, 446–460, Sept., 1955. 6 figs., 32 refs.

Cardiac arrest having occurred during operation 41 times in 4 years at the City Hospital (Western Reserve University School of Medicine), Cleveland, Ohio, with a 63% mortality, the authors were led to investigate in anaesthetized dogs the relative importance of hypercapnia and hypoxia as factors in its causation. They had evidence that in 19 of the 41 cases mentioned inadequate respiratory exchange had played a part.

Mixtures of 55% carbon dioxide or 1% oxygen in nitrogen were insufflated either by tracheotomy or cuffed endotracheal tube into groups of dogs which had undergone bilateral vagotomy, bilateral sympathectomy, or sympathectomy plus bilateral adrenalectomy, and into intact dogs during general anaesthesia with pentobarbitone. At regular intervals the arterial and venous blood pressures, plasma potassium, calcium, and magnesium levels, blood *p*H, and arterial oxygen and carbon dioxide content were estimated; electrocardiograms and electroencephalograms were continuously recorded.

Hypercapnia caused a sharp initial fall in pulse rate and blood pressure followed by a transient rise, after which there was a second, but very gradual, fall. These results were little affected by vagotomy, but after sympathectomy (with or without adrenalectomy) the initial fall was profound and usually caused cardiac arrest within 5 minutes. Concurrently there was a transient rise, then a fall in plasma potassium level, usually followed by a second more gradual rise; the plasma calcium and magnesium levels showed variable changes, and no correlation could be established between them and the pulse rate or blood pressure. Depression of cerebral function, as indicated by the electrical activity of the brain, ran roughly parallel to the curves of pulse and blood pressure. No animal survived after cerebral electrical activity had been absent for more than 20 minutes, even though it might recover temporarily.

Hypoxia caused an initial rise in both pulse rate and blood pressure, after which there was bradycardia with sustained hypertension for a period, followed in turn by a precipitous fall in blood pressure leading to cardiac arrest. When the oxygen content of the inspired mixture was 2, 4, or 8% instead of 1% the effects were less marked, only one out of 6 animals given 8% oxygen having cardiac arrest. The only effect of vagotomy on these phenomena was to smooth out the fluctuations of pulse rate and blood pressure, without affecting the final levels reached. Sympathectomy, however, caused an immediate fall in pulse and blood pressure and earlier cardiac arrest. Less severe degrees of hypoxia continued for long periods were accompanied by a slight fall in the *p*H of the blood and a rise in its potassium content. The plasma levels of the other cations behaved as erratically as in hypercapnia. There was immediate depression of cerebral activity if the oxygen content was less than 4%. In a short series of experiments on 10 human subjects who were given 35% carbon dioxide while under thiopentone anaesthesia, the results were similar to those obtained in dogs and it was noted that in 4 of the cases of cardiac arrest first mentioned bradycardia and hypertension were present before cardiac arrest occurred.

Donald V. Bateman

1053. **Relationship between per cent of Carbon Dioxide in Inspired Air and Degree of Bronchoconstriction**

R. M. Peters. *Annals of Surgery* [*Ann. Surg.*] **142**, 461–468, Sept., 1955. 4 figs., 12 refs.

Earlier work by the author having shown that hypercapnia causes bronchoconstriction, he now reports further experiments carried out at the University of North Carolina School of Medicine to demonstrate a quantitative relationship between the two, if present. Anaesthetized dogs rendered apnoeic with succinyl choline were ventilated through a tracheotomy opening by a pump. A wide thoracotomy was then performed and the phrenic nerves crushed. Carbon dioxide in concentrations ranging from 5 to 25% was supplied from the pump, and a side-tube from the circuit conveyed to a spirometer that part of the gas mixture displaced when bronchoconstriction occurred.

At and above a concentration of carbon dioxide of 10% bronchoconstriction occurred consistently and the slope of the curve recorded on the spirometer kymograph demonstrated a linear relationship between degree of constriction and level of hypercapnia. After periods ranging from 3 to 6 minutes the reflex showed some fatigue, and at any time it could be suppressed by either vagotomy or administration of atropine.

The author suggests that this reflex may play a part in the bronchoconstriction of cardiac asthma since there is evidence that arterial carbon dioxide tension may rise at night. It is also probably active in episodes of bronchoconstriction during anaesthesia following periods of carbon dioxide build-up. Neither in such cases in man nor in the experimental animal do skeletal muscle relaxants have any effect.

Donald V. Bateman

Radiology

1054. **Response of Human Beings Accidentally Exposed to Significant Fall-out Radiation**
E. P. CRONKITE, V. P. BOND, R. A. CONARD, N. R. SHULMAN, R. S. FARR, S. H. COHN, C. L. DUNHAM, and L. E. BROWNING. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 430–434, Oct. 1, 1955. 7 figs., 12 refs.

The explosion of a hydrogen bomb in the Marshall Islands in 1954 resulted in unexpected human casualties due to radioactive dust falling on several inhabited islands. It is stated that " the fall-out material consisted of pulverized and incinerated coral (calcium oxide) coated with radioactive fission products ", its fall being described as " snow-like " or " mist-like ". Among those exposed significant whole-body gamma irradiation was accompanied by skin contamination, and some radioactive material was inhaled and ingested. The calculated whole-body dosage for four island groups ranged from 175 r to 14 r, and the effects of the highest exposures on 64 Marshall islanders in the Rongelap Islands are described in detail.

Less than 24 hours after the explosion two-thirds of the population developed nausea lasting 48 hours. Vomiting and diarrhoea occurred in 10%, and many had itching and burning of the skin and eyes, sometimes with lacrimation. Compared with control subjects from the unexposed Marujo Islands those exposed showed a fall in the lymphocyte count to 25% of the normal level within 3 days, the count remaining at this low level throughout the initial period of study (10 weeks). The neutrophil granulocyte count fell to 70% of control values during the 2nd week and thereafter fluctuated until a second depression to 50% of control values occurred about the 5th week. The count remained at 75% of control values from the 7th to the 10th weeks. The platelet count fell to 30% of control values during the 4th week, by which time 20% of the population had a platelet count below 90,000 per c.mm. The platelet count increased during the 5th and 6th weeks, with a second depression to 70% during the 7th and 8th weeks, this level persisting to the end of the period of observation. Though 11 persons had platelet counts between 35,000 and 65,000 per c.mm., none developed haemorrhage into tissues. Six months after the explosion the blood counts showed little improvement on the 10th-week readings. Twelve months after the explosion the figures for all blood elements had improved, but only the neutrophil count had returned to normal levels. The authors conclude that the group studied received whole-body radiation in a dose about 50 to 100 r short of the level at which some fatalities would have resulted.

Skin and internal radioactive contamination was considered not to have affected the blood findings. The dosage of beta radiation to the skin could not be calculated but " was sufficient to produce epilation and widespread lesions of the skin " in 90% of the group, beginning 12 to 14 days after exposure. Epilation was much commoner in children. Protection was afforded by clothing or shelter, and by bathing during the fall-out period. Hair of normal colour and distribution returned in 2½ to 6 months. Most of the skin lesions were superficial, with dry desquamation leaving depigmented areas. Deeper lesions occurred in 20% of the group, especially on the feet, scalp, neck, and ears, and healed with varying degrees of skin atrophy.

Radiochemical analysis of the urine indicated that internal absorption was roughly proportional to the concentration of air-borne fission products. The internal radiation dose was considered too small to have contributed significantly to the acute radiation syndrome. The authors believe that " the concentration and type of internal radioactive contaminants minimize the probability of any significant long-term effects from the internal radiation ". [No reason is given for this sanguine conclusion.] *E. C. Easson*

1055. **Studies on Nagasaki (Japan) Children Exposed *in utero* to the Atomic Bomb. A Roentgenographic Survey of the Skeletal System**
W. W. SUTOW and E. WEST. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **74**, 493–499, Sept., 1955. 19 refs.

A roentgenographic survey of the skeletal system was made on 74 children who were exposed *in utero* to the atomic bomb explosion in Nagasaki, Japan, at distances under 2,000 meters from the hypocenter. The findings were compared with those on a group of 91 children also exposed while *in utero* to the bomb but at distances of 4,000 to 5,000 meters. No differences in the incidence of skeletal abnormalities were found between the two groups.—[Authors' summary.]

1056. **Effect of Certain Substances on the Permeability of Irradiated Tissues.** (Снижение проницаемости облученных тканей при некоторых веществ)
P. N. KISELEV and P. A. BUZINI. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 17–26, No. 5, Sept.–Oct., 1955. 8 refs.

One of the authors has previously demonstrated that the permeability of tissues temporarily increases following irradiation with *x* rays or radium. In the present investigation the experiments were carried out on the blood–aqueous barrier in rabbit's eyes. The animal was first immunized against the Breslau bacillus, and the normal permeability of the blood–aqueous barrier in the animal's eye to the specific gamma-globulin antibodies which formed as a result of the immunization was then used as a basis for comparison in the subsequent tests. In these, one eye only of the animal was irradiated with *x* rays in doses varying from 100 to 800 r, the permeability of the blood–aqueous barrier in the

irradiated eye for the specific antibodies being then determined in each instance.

The experiments conclusively proved that irradiation weakened the barrier, and it is known that a similar weakening also occurs in inflammatory conditions. The substances tested, which were given intravenously or subcutaneously, included glucose, saccharose, calcium chloride, " citrin " (vitamin P), ascorbic acid, and hyaluronic acid. Small doses of calcium chloride had no effect on the barrier, but larger doses definitely weakened it. Glucose and saccharose had no effect and ascorbic acid generally had but little effect. But citrin and hyaluronic acid given separately, or even more so in combination, definitely strengthened the blood–aqueous barrier in animals which had been subjected to irradiation or were suffering from an infection.

The authors therefore recommend the use of citrin (vitamin P) or hyaluronic acid as a means of strengthening the permeability barrier in tissue following irradiation or in inflammatory conditions. *A. Orley*

RADIODIAGNOSIS

1057. **Pharmacological Studies on Lead E.D.T.A.**
B. J. CLARK and E. G. TOMICH. *British Medical Journal* [*Brit. med. J.*] **2**, 831–832, Oct. 1, 1955. 1 ref.

The possible use of lead ethylenediamine tetraacetic acid (EDTA) as a contrast medium and the administration of the disodium complex intravenously to 4 human subjects have been described by Sapeika (*Brit. med. J.*, 1955, **2**, 167; *Abstracts of World Medicine*, 1956, **19**, 170). In view of this report the present authors describe experiments carried out by them in 1953 on mice, rats, and rabbits, and add the results of some more recent work. They found that the disodium complex did not appear unduly toxic to mice and rats and did not cause haematuria, but its effect on rabbits was disturbing, doses of 1 g. per kg. body weight proving fatal, and smaller doses producing haematuria and severe hepatic and renal damage. As a result of these experiments the authors conclude that a clinical trial of lead EDTA would not be justified, and that the substance is unsuitable for use as a contrast medium. *Kenneth A. Rowley*

1058. **Bronchography with Dionosil**
G. H. C. JOYNT and L. R. HARNICK. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **101**, 425–430, Oct., 1955. 6 figs., 6 refs.

" Dionosil " has now become the contrast medium of choice for bronchography, principally because it is rapidly eliminated from the lungs. It is an ester closely related to diodone, and is available as a 50% suspension in either water or arachis oil. In experiments on dogs at the Banting Research Foundation, University of Toronto, the properties of both suspensions were compared with those of " lipiodol ". With all 3 preparations there was an acute inflammatory response in the lungs following bronchography. With the watery suspension of dionosil the lungs returned to normal within 4 weeks, but when lipiodol or " dionosil oily " was used patchy areas of atelectasis and granulomata were seen in many cases. From these experimental findings the authors conclude that 3 or 4 weeks should elapse between bronchography and segmental resection. The watery suspension, which is obviously safer than dionosil oily despite its slightly greater irritant property, was used by the authors for over 900 bronchograms. *D. E. Fletcher*

1059. **Visciodol in Bronchography**
J. J. BURRASCANO. *Sea View Hospital Bulletin* [*Sea View Hosp. Bull.*] **15**, 149–189, July, 1955. 17 figs., bibliography.

The advantages and disadvantages of the various contrast media at present used in bronchography are discussed at some length. A new contrast medium, " visciodol ", which is a suspension of powdered sulphanilamide in 40% iodized oil, has been tried at the Sea View Hospital, Staten Island, New York, excellent bronchograms being obtained in 40 patients, 29 of whom were tuberculous. The powdered sulphanilamide acts as a thickening agent and gives the medium a high viscosity, thus minimizing alveolar penetration and promoting rapid elimination of the oil. It is non-irritating and its progress along the bronchi is slow, allowing ample time for positioning and filling.

The author describes his technique for bronchography, in which sedation with local anaesthesia is given and various types of Metras catheters are used for introducing the medium. He points out that the basal branches of the right lower lobe are more clearly seen in the left anterior oblique view than in a true right lateral view. In some cases for purposes of comparison visciodol was used for one lung and another medium for the opposite lung, follow-up bronchograms being taken to ascertain the rate of absorption. The author considers that in most cases visciodol is the medium of choice for bronchography. *Sydney J. Hinds*

1060. **A Preliminary Enquiry into the Relative Value of Miniature (70-mm.) Films and Large Films in the Radiological Diagnosis of Pulmonary Tuberculosis**
C. CLAYSON, H. W. O. FREW, D. G. MCINTOSH, J. G. MCWHIRTER, P. L. MCKINLAY, and L. STEIN. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 81–101, April, 1955. 4 figs., 7 refs.

The objects of the investigation described herein were: (1) to compare the efficacy of 70-mm. radiography with that of standard radiography in the diagnosis of pulmonary tuberculosis; and (2) to assess the variation between the interpretations of different observers and of the same observer at different times. A series of 295 large and miniature radiographs were examined, including a high proportion taken in cases of tuberculosis, the number of abnormal radiographs in different batches being deliberately varied. A standard classification was used, lesions being divided into " minimal " and " other stages ", and minimal lesions subdivided into " soft " and " hard ".

A comparison of single and double reading of miniature radiographs showed that the most efficient way of detecting lesions was to double-read the small radio-

graphs, and to re-examine with large radiographs (also double-read) in cases recalled by both observers. By this method 82% of active lesions and 86% of clinically significant lesions were detected. These results were similar to those obtained by single reading of large radiographs, but not so good as those obtained by independent double reading of large radiographs. The authors had great difficulty in attempting to assess the activity of a lesion from a single radiograph.

It is suggested that radiographs of all patients attending chest clinics should be read independently by two observers, and that in the routine work of such clinics it may be more economical to use large radiographs at the outset rather than to spend time in interpreting miniature ones. *T. M. Pollock*

1061. The Significance of the Lateral Subsegments of the Lung in Pulmonary Disease. A Review of 500 Cases. [In English]

L. Di Guglielmo and B. Bonomo. *Acta radiologica* [*Acta radiol. (Stockh.)*] **44**, 217–229, Sept., 1955. 10 figs., 25 refs.

On the basis of a study at the University Institute of Radiology, Pavia, and Södersjukhuset, Stockholm, of 500 cases of various segmental pulmonary lesions the authors discuss the frequency of involvement of the lateral subsegments of the lung. Of their 500 cases, a lateral segmental lesion was found in 23% in various diseases, being situated in the upper lobe in 11·1%, in the middle lobe in 4·9% and in the lower lobe in 7·1% of cases. In the lower lobe a lateral situation rarely occurred in the apical region(1·09%), whereas at the base it was much more frequent (6·1%), particularly in the left lung. The axillary region of the upper lobe was completely involved in 46 cases; the anterior part was affected in only 3 and the posterior part in 4.

The authors give various explanations for the true or apparent involvement of the whole of the axillary area of the upper lobe. In the first place they claim that in from 10% to 18% of cases there is a fourth autonomous segmental bronchus, the lateral bronchus, ventilating this portion of the lung. Studies by Boyden and Scannell (*Amer. J. Anat.*, 1948, **82**, 27) have shown that in cases where there is no lateral bronchus of independent origin the posterior axillary branch in 26% of cases is displaced in such a way that its axis lies over the crossing of the fissures, thus also aerating the area above the horizontal fissure. In 18% of the cases this also occurs in respect of the lateral ramifications of the anterior branch, which thus aerates the surface above the oblique fissure.

The existence of an autonomous lateral bronchus in the middle lobe has been acknowledged by most workers. On the left side the lingular bronchus usually divides into an upper and a lower branch, while the lateral branch originates as a subsegmental ramification of either of these. However, in about 30% of cases the lingular bronchus may also divide into an anterior and a lateral branch.

In regard to the lower lobe, as already stated the apical region is, as a rule, involved as a whole and involvement of the lateral part only is comparatively rare. The possibility that an axillary bronchus may sometimes originate directly from the lower-lobe bronchus has been conceded. The present authors' observations show that the lateral region of the base of the lower lobe on the right as well as the left side is quite frequently (6·33%) the seat of various morbid processes, and that such lesions have well-defined radiological features which generally render their exact location possible. In the postero-anterior projection the opacity appears as a bundle or triangle situated in the lower third of the lung, extending from the hilum to the lateral thoracic wall. It is separated from the diaphragm by normally translucent parenchyma. In the lateral projection the opacity has regular margins, is very dense, lies below the hilum, and is frankly median. Its anterior, superior margin is formed by the oblique fissure, while the posterior, superior margin lies just below the apical part.

L. G. Blair

1062. Correlation of Certain Bronchographic Abnormalities Seen in Chronic Bronchitis with the Pathological Changes

L. M. Reid. *Thorax* [*Thorax*] **10**, 199–204, Sept., 1955. 8 figs., 7 refs.

In the bronchogram of patients suffering from chronic bronchitis Simon and Galbraith (*Lancet*, 1953, **2**, 850; *Abstracts of World Medicine*, 1954, **15**, 363) have described changes at the periphery of the bronchial tree. These consist in failure of filling and the frequent occurrence of small pools of opaque medium in association with the smaller bronchi. In order to correlate these changes with the microscopical appearances in sections of lung tissue the author, working at the Brompton Hospital, London, has devised a special technique in which a necropsy or operation specimen of lung is injected with opaque medium which solidifies. A radiograph is made and by a parallax method the depth of any given lesion can be accurately estimated. Serial sections are then made at about this level and these can be examined microscopically. The author describes and discusses the principal changes as seen in specimens of lung tissue from 11 patients with chronic bronchitis.

(1) When there is failure of peripheral filling bronchioles may show a sudden " cut-off "; this may be due to the presence of secretion which prevents complete filling, or simply to insufficient opaque medium. Contrasted with this is the frequent presence in disease conditions of irregularly tapered and distorted endings of finer bronchi. Microscopy shows that these regions correspond with a region of alveolar collapse or fibrosis. (2) In peripheral pooling the small rounded " pools " of opaque medium which occur as buds on the smaller bronchi are shown to be dilated bronchioles. These are also associated with areas of atelectasis. (3) The third type of abnormality consists in small lateral " spikes " or thorn-like projections from the peripheral small bronchi; there also were found to be terminal or near-terminal bronchioles cut off by atelectasis of lung or fibrosis. Some of these spikes showed varying degrees of dilatation, resulting in transition forms of the " pools " already described.

The author considers that the study of good bronchograms in cases of chronic bronchitis will yield information about the chronicity of the disease and the degree of irreversible change which may be present in the lung—changes which, owing to the small size of the lesions, may not be manifest in the plain radiograph.

A. M. Rackow

1063. **The Detection of Carcinoma of the Lung by Screening Procedures, Particularly Photofluorography**
L. H. GARLAND. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **74**, 402–414, Sept., 1955. 1 fig., 32 refs.

[In the U.S.A. the term screening implies a different procedure from that commonly understood in Britain.]

In this paper from Stanford University, California, a screening procedure is defined as a " preliminary diagnostic examination applicable primarily to asymptomatic persons ". The most frequently used screening procedure for the detection of carcinoma of the lung is *x*-ray examination, employing single anterior exposures made in full inspiration on a 70-mm. radiograph, but other techniques are briefly discussed. The author points out that the size of the radiograph is of less importance than the experience of the observer, but that even experienced observers miss about 27% of " positive " radiographs. The types of pulmonary lesion likely to be overlooked are listed.

Much of this paper is devoted to analyses of the results of various chest surveys for bronchogenic carcinoma, particularly of photofluorographic screening procedures, carried out by others in the U.S.A. One significant conclusion is that the prognosis in survey-detected cases of bronchogenic carcinoma is little better than that in cases detected by conventional methods of examining the chests of apparently symptomatic subjects.

Sydney J. Hinds

1064. **Roentgen Diagnosis of Esophageal Varices. Comparison of Roentgen and Esophagoscopic Findings in 502 Cases**
I. E. KIRSH, C. C. BLACKWELL, and H. D. BENNETT. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **74**, 477–485, Sept., 1955. 6 figs., 17 refs.

For the purpose of establishing the relationship between Laennec's cirrhosis and oesophageal varices, *x*-ray examination of the oesophagus and oesophagoscopy were carried out at the Veterans Administration Hospital, Hines, Illinois, on 502 patients in a recent 4-year period. This investigation provided an opportunity for a controlled evaluation of the two diagnostic procedures, which is reported in this paper.

The contrast medium used for *x*-ray examination consisted of 4 oz. (113 g.) of barium sulphate in 2 oz. (57 ml.) of water, with the addition of 0·25% carboxymethylcellulose. With the patient recumbent 3 radiographs were taken—an inspiratory and an expiratory in the right anterior oblique position and one in the left anterior oblique position with the Valsalva manœuvre. The patient was also screened and spot films, for which a thinner barium mixture was used, were taken. The criteria for diagnosis and differential diagnosis are discussed.

The authors state that for the purposes of this report the findings at oesophagoscopy were taken as correct. On this basis the findings on *x*-ray examination were in agreement with those of oesophagoscopy in 454 (90%) of the 502 cases.

Sydney J. Hinds

1065. **Diagnostic Pneumoperitoneum**
S. C. TRUELOVE and K. LUMSDEN. *British Medical Journal* [*Brit. med. J.*] **2**, 585–588, Sept. 3, 1955. 6 figs., 6 refs.

The authors of this paper from the Radcliffe Infirmary, Oxford, have found that an artificial pneumoperitoneum is of considerable help in the radiological examination of the abdominal organs, particularly as regards the gross morbid anatomy of the liver and spleen. Air is very readily introduced into the peritoneal cavity in cases of ascites, and the introduction of 1 to 2 litres after withdrawal of ascitic fluid causes no discomfort. In patients without ascites the technique is similar to that used in the treatment of pulmonary tuberculosis.

The *x*-ray examination is best carried out with the patient in the prone position, movement of the air for outlining a particular organ being readily obtained by rotating the patient. The liver and spleen are usually seen very clearly. Brief reports are given of cases in which this procedure was used, including cases of alcoholic and biliary cirrhosis, peritoneal metastases, retroperitoneal tumour, and one case of pleural effusion in which the radiograph suggested a high diaphragm. The authors advocate the routine use of this method in any case of ascites in which the diagnosis is in doubt, because the refill is simple to carry out after paracentesis. In many cases pneumoperitoneum may be performed with little risk or disturbance to the patient and may yield valuable information.

A. M. Rackow

1066. **The Use of Morphine and Propantheline in Intravenous Cholecystography**
A. J. SANGSTER. *Lancet* [*Lancet*] **2**, 525–527, Sept. 10, 1955. 2 figs., 9 refs.

The value of " biligrafin " as a contrast medium in investigations of the biliary tract, particularly in patients who have undergone cholecystectomy, is now well established. However, the density of the shadow is disappointing in some cases, this being due either to disease of the liver, in which case the medium is eliminated chiefly by the kidneys and the resulting pyelogram will indicate impaired liver function, or to very rapid passage of the medium into the duodenum. As regards the latter it has been shown that injection of morphine causes the sphincter of Oddi to close within 5 minutes and that visualization of the hepatic ducts is thereby much improved. The present author describes the technique of examination he has used in 66 cases at Raigmore Hospital, Inverness, in which $\frac{1}{6}$ grain (11 mg.) of morphine was given intravenously 30 minutes after slow intravenous injection of 40 ml. of biligrafin. In some cases the resulting spasm of the sphincter of Oddi caused pain, but intravenous injection of 30 mg. of propan-

theline bromide relieved the pain and released a flood of medium into the duodenum. *Sydney J. Hinds*

1067. **Radiographic and Other Studies of the Biliary and Pancreatic Ducts**
H. WAPSHAW. *British Journal of Surgery* [*Brit. J. Surg.*] 43, 132–141, Sept., 1955. 11 figs., bibliography.

At the Western Infirmary, Glasgow, the author studied the cholangiograms obtained in 56 patients suffering from disorders of the biliary system or pancreas. The contrast medium was " neo-hydriol fluid " or " pyelosil 70 ", the former being preferred. The ducts were injected either at operation or, through a drainage tube, 8 to 10 days after operation. Variations in the pattern of the normal cholangiogram are discussed.

Reflux of the contrast medium into the pancreatic duct occurred for a variable distance, making the duct visible in the radiograph in 7 cases in the series. The author discusses the possible causes of this, and quotes others who have found pancreatic reflux in a somewhat higher proportion of cases. The most probable cause is an anatomical one, the two ducts becoming conjoined proximal to the sphincter of Oddi. There was some evidence that acute pancreatitis, by lowering the secretory pressure of the pancreas, was also a factor.

The effect on the sphincter of Oddi of injection of morphine at or immediately before cholangiography was studied in 23 patients. In 18 the effect was similar to spasm of the sphincter, which came on at times varying from 4 minutes to 2 hours after administration of the morphine. The author considers this to be due to increased tone in the duodenal wall rather than to spasm of the sphincter itself. In those cases in which reflux into the pancreatic duct had been seen the effect was to dissociate the two ducts.

The management of cases in which stones in the cystic or common bile duct are not detected at operation is discussed. The cholangiogram may be confusing because of the presence of translucencies caused by blood clots or other organic debris, or by air bubbles. When stones are detected in the cholangiogram after operation they should be removed without further surgery; the author discusses the use of ether, antispasmodics, and oil for this purpose.

Undesirable effects of cholangiography, as reported by other authors, include cholangitis and, probably, pancreatitis. Neither of these occurred in the author's series of cases, but there was one instance of temporary collapse which was attributed to over-distension of the gall-bladder. *A. M. Rackow*

1068. **Roentgen Examination of the Abdomen in Acute Pancreatitis**
W. F. BARRY. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 74, 220–225, Aug., 1955. 10 figs., 8 refs.

Some reports in the literature on the radiological appearances of the abdomen in cases of acute pancreatitis describe localized regions of ileus in the stomach, small intestine, or colon. At the Veterans Administration Hospital, Richmond, Virginia, plain radiographs of the abdomen were obtained in 19 out of 40 cases in which acute pancreatitis was diagnosed. In 12 of these 19 there were features which were highly suggestive of the diagnosis; 4 cases are described in detail and illustrated.

Characteristically, the radiograph revealed loops of gas-filled small bowel in the left upper quadrant; in some instances these were also seen in the mid-abdomen. The duodenal loop might be dilated, and this was best seen in the postero-anterior radiograph taken with the patient lying in the left lateral decubitus position. Gas-filled loops and fluid levels might also be observed in the large intestine, notably in the ascending or transverse portions. In some cases the stomach was dilated with air. These abnormalities were noted 6 hours to 4 days after the onset of symptoms, the optimum time being 12 to 48 hours after the onset.

A. M. Rackow

See also Urogenital System, Abstract 953.

RADIOTHERAPY

1069. **The Treatment of Cerebellar Medulloblastoma in Children.** (О лечении медуллобластом мозжечка у детей)
I. S. BABTCHIN and E. M. GOL'TSMAN. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] 19, 8–13, No. 5, Sept.–Oct., 1955. 8 refs.

The authors, working at the Neurosurgical Institute, Leningrad, report some encouraging results from the treatment of medulloblastoma in 14 children by a combination of surgery and radiotherapy. The latter is applied not only to the tumour but is also directed at the lateral ventricles and the spinal cord, being best administered in several courses; details of methods of application and dosage are given. The results over a follow-up period varying from 1 to 4 years were encouraging, only one child returning with symptoms of metastatic spread of the tumour to the spinal cord.

L. Crome

1070. **The *X*-ray Therapy of Medulloblastomata.** (Рентгенотерапия медуллобластом)
N. S. PLEVAKO. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] 19, 14–19, No. 5, Sept.–Oct., 1955. 1 fig., 1 ref.

The author reviews the results of treatment of 90 cases of medulloblastoma at the Burdenko Institute of Neurosurgery, Moscow, with a combination of complete or partial resection and *x*-ray therapy. The average period of survival for the series was 2 years, and 7 of the patients were alive at the time of writing, 2½ to 3 years after operation. Earlier results with small doses of *x* rays had been less satisfactory; the author's present policy therefore is to give several courses, each of up to 3,000 r, to a total of 12,000 to 15,000 r. Except in cases of metastasis the spinal cord is not irradiated, since in his view it is undesirable to expose the internal organs such as the liver, spleen, and parathyroid glands to irradiation.

L. Crome

1071. **Estrogen and Combined Estrogen and *X*-ray Therapy. Their Effects on Advanced Malignant Salivary-gland Tumors**

G. WHITE and G. G. GARCELON. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 410–412, Sept. 8, 1955. 4 refs.

Oestrogens with and without irradiation were tried in 8 cases of advanced malignant disease of the salivary glands at the Pondville Hospital, Walpole, Massachusetts, and the Veterans Administration Hospital, Boston. Diethylstilboestrol was given in a dosage of 10 to 40 mg. daily for one week to 7 months. With this treatment alone there was improvement in 3 cases, in one of which metastases regressed completely. Subsequently 7 of the patients received irradiation, the dosage ranging from 1,500 r measured in air in 5 days to 6,800 r in a period of 24 days. Improvement was observed in all 7 cases. It is suggested that hormone therapy should be carried out for one month before irradiation is considered, so that any beneficial effect can be assessed; irradiation should be given when signs of reactivation occur. It is observed, however, that some of these salivary tumours might have responded equally well to irradiation alone. *Kenneth Gurling*

1072. **Treatment of Malignant Serous Effusions with Radioactive Colloidal Chromic Phosphate**

H. L. JAFFE. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **74**, 657–666, Oct., 1955. 13 figs., 2 refs.

From the results obtained at the Cedars of Lebanon Hospital, Los Angeles, in 50 cases of serous effusion associated with malignant disease an assessment is made of the value of treatment with radioactive phosphorus (^{32}P) in the form of colloidal chromium phosphate in place of radioactive gold (^{198}Au). If the effect of ^{198}Au is due to its emission of beta radiation only, then ^{32}P, emitting pure beta radiation, should be equally effective. The elaborate protective measures necessary in handling ^{198}Au owing to its gamma radiation are unnecessary with ^{32}P, with consequent reduction in the transport costs and irradiation risk to staff. The longer half-life of ^{32}P (14·3 days) reduces loss in transit, facilitates storage, and increases availability.

A plastic-covered syringe taking glass cartridges is used for administration, the isotope being supplied and stored in the cartridges, which can be discarded after use. Polythene tubing is inserted into the pleural cavity through a needle, which is then withdrawn. Aspiration and injection are carried out through this tube, which may then be clamped and stitched *in situ* for use if subsequent drainage is necessary, this being possible without loss of the isotope, which becomes fixed to the serous surfaces within 72 hours. Doses ranging from 5 to 30 mc. in a single injection have been tried, but radiation sickness, pleuritis, and peritonitis of short duration were experienced with the higher doses. The present treatment schedule is 5 mc. per injection, this being repeated up to a total of 6 times at intervals of 3 to 7 days, depending on the response. [This interval would appear to be too short in view of the half-life of 14·3 days.]

Of 30 cases of pleural effusion treated, improvement was obtained in 20, while of 20 cases of ascites treated, improvement was obtained in 12. Improvement was obtained in cases secondary to cancer of the breast, ovary, lung, and stomach, and (in one case) to lymphosarcoma. [Criteria of improvement are not given.]

The conclusion is reached that radioactive chromic phosphate is as effective as radioactive gold for this form of palliation, and much more convenient to use.

J. Gordon Stewart

1073. **Radiotherapy of Bladder Cancer by Means of Rubber Balloons Filled *in situ* with Solutions of a Radioactive Isotope (Co^{60})**

J. H. MULLER. *Cancer* [*Cancer (N.Y.)*] **8**, 1035–1043, Sept.–Oct., 1955. 4 figs., 18 refs.

The author describes, from the University of Zürich, his latest technique of intracavitary radiation, using liquid solutions of radioactive cobalt (^{60}Co) chloride to give a homogeneous distribution of radiation. The chief advantage of this isotope lies in the practically monochromatic (that is, of one single wavelength) gamma radiation (average 1·2 meV) and the soft beta rays (0·3 meV) which are readily absorbed by thin material. It has an important advantage over single central sources in that serious unbalancing of dosage can be avoided; in a 75-ml. sphere a shift of 0·7 cm. of a central source gives a 3 to 1 variation of dose on opposite sides, whereas even substantial variations from the perfectly spherical form of a liquid source cause only minor differences. The chief disadvantage is the danger of spill; this occurred in 2 of the author's cases, with systemic absorption, but with no serious consequences. Home-made balloon catheters have been replaced by " bardex " type inserted per urethram. A trial filling is made with water, a contrast medium, and a dye to test its tightness and the patient's ability to retain it for 8 to 24 hours, and a radiograph is taken. If satisfactory, and no stained urine is seen, the contents are replaced by ^{60}Co. The results are best with a volume of 70 ml.; larger volumes increase the depth dose, but also the risk of late fibrotic contracture of the bladder wall. The required dosage is about 10,000 r ($\pm 20\%$) at the outer balloon surface. Deeply infiltrating growths are not very suitable for this technique. In a typical case 20 mc. is left in the bladder continuously for a week, or up to 10 days for lesser amounts; intermittent treatment may be needed if the patient does not tolerate it well or if there are signs of leakage. Graphs are presented to show dosages at up to 3 cm. from the surface, for both a fluid and for a central source. The relatively small amounts of radioactive material permit fairly simple filling devices.

Between 1948 and 1954, 96 cases have been treated. It is essential to combine surgical treatment in many cases, for example, resection of large papillary growths or partial cystectomy, in order to increase the range of curative penetration; but deep electrocoagulation is to be avoided as tending to weaken the mechanical strength of the bladder wall. The most favourable types of tumour for treatment are the superficial and the histologically well-differentiated. Reactions were negligible

in half the cases; the other half showed mild or severe chronic cystitis. About one year after treatment there is a risk of late mucosal necrosis, which is usually superficial and heals slowly. Any infection present must be thoroughly treated with sulphonamides and antibiotics. Even if cystectomy eventually becomes necessary the prospects are improved by the preoperative irradiation and the technical difficulty of surgery is not increased. Of the author's 96 patients, 41% are symptom-free at up to 3½ years. Tables of results are given, showing the histology and complications in each case.

[The technique here described may be compared and contrasted with the central-source method as used at Manchester and outlined by Bratherton (see Abstract 1074).] *J. Walter*

1074. **The Treatment of Bladder Growths by a Solid Intravesical Cobalt Source**

D. G. BRATHERTON. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 508–513, Sept., 1955. 10 figs.

In this discussion from the Christie Hospital and Holt Radium Institute, Manchester, of methods of treatment of neoplasm in the urinary bladder the author states that early growths are best treated by radon-seed implants, more advanced infiltrating growths by deep *x* rays, but between these two types are cases of multiple superficial growths for which an intravesical source of rays is better. Both liquid and solid radioactive sources are available; a solid source avoids the dangers of spill and contamination, is always ready for use, and gives the best depth dose. The chief technical difficulty is in ensuring the central positioning of the source, since an eccentricity of a few millimetres can lead to serious unbalancing of dosage on the surface. To this end, special latex bags have been developed which are easily inserted per urethram on a rigid metal catheter; they are provided with channels for inflation, and for continuous suction drainage of the urine in order to maintain apposition to to bladder wall. The bag is filled with 5% sodium iodide (for radiographic visualization) plus a dye (fast green) to detect leakage into the urine. Since radium sources were found too large for insertion 2 " slugs " of radioactive cobalt were used, each of 80 mg. radium equivalent, giving 3000 r in 24 hours on the surface of a sphere of 150 ml. volume; 200 ml. gives better depth dose but needs longer time.

The bag is inserted under anaesthesia, filled from a syringe, and checked for shape and position on a radiograph; if the shape is not satisfactory, the bag is removed and another tried. In the ward the suction pump is connected and the cobalt inserted; the film is repeated next morning. Only superficial lesions are suitable for this treatment; large masses are first cut down by diathermy. Since the cooperation of the patient is essential, the method is unsuitable for uraemic or confused patients, or those in poor physical condition. A dose of 3,000 r is given, and repeated in one week, to a total of 6,000 r; in the present series 7,000 r was given, but this proved too high. Some patients have discomfort and may have spasm, which can be controlled by pethidine. Penicillin and sulphamezathine are given during treatment and for one day after. Treatment is usually followed by frequency of micturition for 3 or 4 weeks. It is important to clear the bladder of infection first; in this series there was one death from septic cystitis. Growths may take many months to disappear completely; if papillomata do not entirely disappear, their growth is slowed, and they can be lightly touched with diathermy (not deeply cauterized, as the healing powers of the mucosa are reduced).

Of 16 patients with carcinoma of the bladder treated 2 years ago, 8 are still alive, of whom 5 responded well and 3 needed further surgery for recurrence; 8 are dead, 5 of recurrence of the primary tumour, one of infection, and 2 of haemorrhage from telangiectases. Of 12 patients with multiple papillomata 10 are alive at 2 years, but only 2 are well controlled; in 7 cases the lesions were reduced but further diathermy was needed, in one they were uninfluenced, and 2 patients died. Complications included infection, bleeding (probably from overdosage), and formation of stone after diathermy. Contraindications include spread of the growth to the prostatic urethra, reduced capacity below 100 ml., previous *x*-ray or radium treatment, and urethral stricture. Even if cystectomy becomes necessary later 2 or 3 years of life may be gained and nothing is lost. *J. Walter*

1075. **A New Approach to the Treatment of Chronic Leukaemia with ^{32}P**

E. C. EASSON, B. E. JONES, and L. A. MACKENZIE. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 405–409, Aug., 1955. 8 figs., 4 refs.

The authors report that in more than 90% of cases of chronic leukaemia of all kinds treated with radioactive phosphorus (^{32}P) at the Christie Hospital and Holt Radium Institute, Manchester, the fall in the leucocyte count was exponentially related to the integral body dose of radiation received by the patient. In other words, if the integral body dose in millicuries destroyed is plotted daily against the logarithm of the leucocyte count, the points will fall along a straight line. By extrapolating this line to the leucocyte count it is desired to attain, a prediction may be made in each case at an early stage of treatment of the amount of ^{32}P which will be needed. Calculation of the integral body dose has to take the loss of ^{32}P by excretion into account, and a formula for the purpose is given, together with a table of values calculated from this formula from which the integral body dose any number of days after a given dose can be read off.

The authors state that since using this method of prediction they have been able to reduce the average amount of ^{32}P required by about 4 mc. per patient. Strictly, the method applies only to the initial course of treatment in each case, but the response to subsequent courses tends to be similar to that to the first. The authors advise an initial dose of 6 mc., which will enable a satisfactory prediction of the total dose required in that case to be made after 14 days. The necessary extra dose can then be given and the leucocyte count will be found to fall to the required level.

E. Stanley Lee

History of Medicine

1076. **Ergot Poisoning, a Pandemic of the Middle Ages.** (Die Secalevergiftung, eine mittelalterliche Volksseuche) H. O. MÜNSTERER. *Münchener medizinische Wochenschrift* [*Münch. med. Wschr.*] **97**, 1035–1036, Aug. 12, 1955. 3 figs., 24 refs.

The frequency and widespread occurrence of ergot poisoning in the Middle Ages is illustrated by the fact that a hospital order was founded at the end of the 11th century especially for the care of those afflicted. The order grew rapidly, and at one time it had 369 branches all over Europe. According to legend, it was founded in gratitude to St. Antony of Egypt, the patron saint of the Dauphiné, by a French nobleman whose only son had been cured of the disease by the saint's intervention. The disease variously called ignis sacer, *mal des ardents*, and St. Antony's fire was at different times thought to be epidemic herpes zoster, erysipelas, and anthrax, but the predominant symptom of burning pain in the extremities followed by gangrene, which medieval authors describe and sometimes illustrate, leaves little doubt that it was, in fact, ergot poisoning. Its epidemic nature is explained by the periodic infection of grain with *Claviceps purpurea* over wide areas.

The last large epidemic in Europe occurred in Hungary in 1906–7. [There was a small outbreak in France in 1951 (see Giraud and Latour, *Bull. Acad. nat. Méd. (Paris)*, 1952, **136**, 422; *Abstracts of World Medicine*, 1953, **13**, 78)]. Although the disease as originally caused has almost died out it would be wise to keep it in mind in view of the frequent administration of drugs containing ergot over long periods, which may perhaps account for some of the cases of vague and mild paraesthesiae occasionally seen in some patients. *Marianna Clark*

1077. **The Antecedents of Blood Transfer**
L. BLUM and W. M. NELSON. *Bulletin of the New York Academy of Medicine* [*Bull. N.Y. Acad. Med.*] **31**, 671–681, Sept., 1955. 5 figs., 35 refs.

[This brief survey of the history of blood transfusion is extended to include an account of the development of the artificial kidney and the extracorporeal shunt, for which the reader is referred to the original article.]

The idea that vitality, emotion, and heritage could be transmitted by transfusion of blood is of ancient origin. In 1665, at Oxford, Richard Lower performed the first successful transfusions on animals, connecting their blood vessels with quills and silver tubes. Two years later, in Paris, Denis performed the first recorded transfusion on man, the blood of a lamb being transferred directly into the veins of a youth, but the procedure fell into disrepute and was abandoned for the next 150 years.

In 1821 Prévost and Dumas showed that exsanguinated animals could be revived by transfusion, and in 1828 Blundell described 11 cases in which transfusion was performed for postpartum haemorrhage, emphasizing the importance of using human donors. However, the frequency of reactions limited the application of the procedure and it was not until 1901 that Landsteiner described the blood groups and paved the way for the removal of most of the risks of transfusion. The practical application of his work by Ottenberg became part of clinical technique in 1911, but the problem of controlling the physical state of the blood and preventing clotting was not solved until 1914, when Hustin reported the anticoagulant effect of citrate. Although the first citrated transfusion, credited to Luis Agote, was performed in Buenos Aires in the same year, blood banks were not established until 30 years later. [In this respect developments in Great Britain were in advance of those in the U.S., and enabled a large-scale organization for the collection, storage, and supply of blood to be set up in Britain immediately on the outbreak of war in 1939.] *Norman F. Smith*

1078. **The Development of American Anatomy Acts**
J. B. BLAKE. *Journal of Medical Education* [*J. med. Educ.*] **30**, 431–439, Aug., 1955. Bibliography.

Although some Greek physicians, particularly of the Alexandrian school, from about the third century B.C. to the first century A.D. dissected human cadavers, by the time of Galen (*c.* A.D. 130–200) the practice was no longer allowed, and from the fall of the Roman Empire throughout most of the medieval period the dead human body remained inviolate apart from occasional necropsies. This situation obtained up to less than 100 years ago in the United States, and because of popular hostility anatomists were forced to obtain bodies for dissection surreptitiously and many subterfuges were resorted to. But the medical profession was greatly dissatisfied with this state of affairs, and during the 1820s the problem was increasingly ventilated before the public. A movement to legalize the supply of anatomical subjects was advancing contemporaneously in Great Britain, and the American press reflected the furore created by the disclosure of the notorious murders committed by Burke and Hare in 1828.

As a result of this agitation the Massachusetts General Court in 1831 passed America's first real Anatomy Act, which repealed the legislation of an Act of 1815 making possession of a dead body a crime and specifically authorized physicians and medical students to possess cadavers. This law preceded Warburton's Act passed in 1832 in Britain and was a great triumph. Within the next 30 years a number of other States passed similar laws, but mostly repealed them within a few years. Soon after the American Civil War, however, a new period of legislation set in, and in 1881 a survey showed that of the 38 States, 15 had "liberal" Anatomy Acts, 9 had "illiberal" ones, and 14 none at all.

By the turn of the 19th century medicine itself was rapidly rising in the public estimation, and perhaps the most characteristic feature of middle-19th-century medical science was its emphasis on pathology and the differentiation and identification of diseases on the basis of correlated clinical and post-mortem findings. It was at this time that active philanthropy began to finance medicine and public health; Johns Hopkins was an early benefactor, but the classic example was Rockefeller. When the public found medicine worthy of support, support was forthcoming, including the supply of anatomical subjects.

The early difficulties in Britain and the United States showed the public antipathy towards dissection, but also, and more fundamentally, the commercialism of the medical schools and the low esteem in which the public generally held the medical profession. " This story also suggests that when in a democracy medicine finds itself flouting public opinion and neglecting its own best ideals, it is flirting with disaster." *Leon Gillis*

1079. **Philippe Pinel and the English**
A. LEWIS. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 581–586, Aug., 1955. 33 refs.

Pinel is remembered mainly for his pioneer work in improving the care of the mentally ill and delivering them from the neglect, cruelty and physical restraint which were the rule in his day. But his achievements in other fields of science and medicine are also worthy of our attention. For example, he was one of the first to advocate the application of statistical methods to medicine and psychiatry, and had always distinguished himself by a distrust of sterile systems and facile explanations. In his *Traité médico-philosophique sur l'aliénation mentale* he laid down the conditions required for the correct appraisal of any method of treatment in psychiatry, namely, through the statistical study and comparison of carefully made observations of a large number of cases, according to a fixed and regular plan. Pinel owed this interest in the application of the theory of probabilities to his early mathematical training—while a medical student at Montpellier and Toulouse he earned his living partially by giving lessons in mathematics. He was a friend of Condorcet and d'Alembert and was fully acquainted with the works of Borelli and Baglivi.

His intellectual outlook had been indirectly influenced by English thought through the French humanists who derived many of their views from Locke and other English and Scottish empiricists. Furthermore, his acquaintance with the *Philosophical Transactions of the Royal Society*, a selection of which he translated into French, including several papers on vital statistics, confirmed and stimulated his natural inclination towards empirical and mathematical thinking. It is likely that in this particular field Pinel owed more to the English than the English owe to him, and apart from Esquirol, who took up all his teachings on the use of statistics, there is no evidence that he had any direct influence on his successors in France. In England William Farr, John Thurnam of The Retreat, and other advocates of the application of statistics in medicine seem to have been well acquainted with the works of Esquirol, but hardly mention Pinel. English influence is also noticeable in Pinel's psychological concepts, which he took from Locke, Harris, Adam Smith, and Dugald Stewart, either directly, for he read English, or through Condillac. It is often forgotten that besides being a great alienist Pinel was also one of the two most eminent physicians and teachers in Paris of the time, and his *Nosographie philosophique* became a classic not only in France but in the whole of Europe. Pinel died in 1826.

Although The Retreat at York was founded in complete ignorance of the teachings of Pinel, his work at the Hôpital Bicêtre had an influence on the " non-restraint " movement among alienists in England. Gardiner Hill and Conolly quoted and found support in Pinel, more indeed in what he demonstrated in actual practice than merely in the humanitarian theories which he maintained. The man who knew Pinel best of all, Esquirol, called him " the La Fontaine of medicine ". *Richard de Alarcón*

1080. **James Cowles Prichard, M.D., 1786–1848**
D. LEIGH. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 586–590, Aug., 1955. 12 refs.

Many psychiatrists attribute to Prichard the first description of psychopathy. Born at Ross in Herefordshire in 1786, he was educated at Bristol, showing from an early age a great inclination towards and facility for foreign languages. After some time at St. Thomas's Hospital, London, he proceeded to Edinburgh where he graduated M.D. in 1808, and in 1812 he was appointed physician to St. Peter's Hospital at Bristol, a hospital which treated a number of mental and neurological patients. In 1816 he was elected physician to the Bristol Infirmary. Prichard took an active part in the social and intellectual life of Bristol and was a founder of Bristol College and Bristol Literary and Philosophical Society, and President of the Medical Library. A versatile and many-sided man, he wrote works on ethnology, literature, and psychiatry.

Prichard's psychiatric studies, though of considerable interest, are dwarfed by his anthropological and philological works. They consist of three main works; the first, *A Treatise on Diseases of the Nervous System* (1822), is largely a collection of case histories, with some attempt at a broad classification based mostly on that of de Sauvages and Pinel. Of interest is his discussion in it of Pinel's *manie sans délire*, in which he states that all murders committed by lunatics are carried out under some hallucination. In 1835 he published his second work, *A Treatise on Insanity*, which he dedicated to Esquirol. It is a much better constructed book though still showing a marked French influence. In it Prichard separates the " moral insanities " from other types of insanity and insists that they form a specific group. In his third book, *Different Forms of Insanity in Relation to Jurisprudence* (1842), he develops this concept further and subscribes to the idea of " instinctive madness ", a type of mental disorder exemplified in those individuals who, while exhibiting apparently normal external behaviour and full consciousness, are driven by sudden

and really irresistible impulses to commit crimes and other acts of violence. Thus he considered crime on the whole to be linked with mental disorder. Most of the patients he describes as suffering from moral insanity would nowadays be considered as manic-depressives or obsessionals and not really psychopaths.

It is a curious fact that Prichard's ethnological and philological works are much better documented and show much more originality than his psychiatric writings, which suffer from an overwhelming preponderance of French sources, while English and other Continental writers on psychiatry of the time are ignored. His influence on French psychiatry seems to have been negligible, and his medico-legal concepts were entirely ignored by the committee of judges which drew up the McNaughton Rules in 1843. *Richard de Alarcón*

1081. **Dr. W. A. F. Browne**

J. HARPER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 590–593, Aug., 1955.

William Alexander Francis Browne, the son of an Army officer, was born and educated at Stirling, studied medicine at Edinburgh, where he qualified in 1826, and then spent 2 years on the Continent, mainly in France, where he studied under Esquirol. In 1834 he was appointed Medical Superintendent of Montrose Asylum in Angus, Scotland. Fired by the example of Pinel and Esquirol and the work of the Sisters of St. Vincent de Paul in France he set himself as his aim in life to improve the conditions in which the mentally ill were kept at that time. He started this task at Montrose and soon published a book, *What Asylums Were, Are and Ought to Be*, in which not only did he criticize the neglect and cruelty then prevailing in most mental hospitals, but gave besides many valuable suggestions for the improvement of these conditions.

When the Crichton Royal Institution near Dumfries was founded in 1838 Browne was appointed its first Resident Medical Officer. He remained there for 18 years and was able to put into practice many of the ideas and reforms he had suggested in his book. From the beginning patients were encouraged to take part in a variety of social and recreational activities, soon published a monthly periodical, *The New Moon*—the first of its kind—written by themselves, and private theatricals were organized as a form of therapy. Browne, being also an excellent clinician, realized the importance of systematic observation and detailed clinical records. As early as 1842 he started recording the dreams of his patients and also commented on the significance of behaviour disorders in children. He was a strong supporter of non-restraint, and convalescent patients were allowed great freedom with the aim of helping them in their readjustment to normal life. He was also concerned with the training of an adequate nursing staff and in 1854 instituted a course of 30 lectures on insanity for his nurses to whom, as he pointed out, had to be committed in great measure the management and day-to-day treatment of the patients.

As senior Medical Commissioner in Lunacy for Scotland—he was at last persuaded to leave Crichton Royal to take up this post—he was, according to a contemporary, " mainly instrumental in formulating the liberal and enlightened policy of the New General Board of Lunacy in Scotland " and did much for the improvement and building of lunatic asylums and the introduction of better methods of treatment. *Richard de Alarcón*

1082. **A Note on James Parkinson as a Reformer of the Lunacy Acts**

W. H. MCMENEMEY. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 593–594, Aug., 1955. 4 refs.

At the beginning of the 19th century in England there existed only the Lunacy Act of 1744 which permitted two magistrates to apprehend and fetter a lunatic, and later the Act of 1774 allowing the granting of licences to all who wished to keep madhouses. Five Fellows of the College of Physicians constituted a Board of Commissioners, who had powers of inspection but, having no power of punishment, were virtually useless and generally ignored. The names of Wynn, George Rose, Henry Brougham, Thomas Wakley, and Lord Ashley are usually mentioned in connexion with the reform of the lunacy laws within Parliament, but it is of interest and worthy of notice to see how James Parkinson, the apothecary of Hoxton, though not a psychiatrist, played a small but important part in encouraging these reforms through his book *Observations on the Act for Regulating Madhouses* and to recall the circumstances that led to his writing and publishing it.

In 1807 he was asked by her nephew to examine a widow named Mary Daintree, who had been in the habit of wandering about the street at night, had openly blamed herself for her husband's death, and was considered suicidal. Parkinson examined her carefully, interrogated her son and her neighbours, and agreed that she should be committed to an asylum. After she had been certified for a time she was released through the efforts of a friend, on the grounds that she was no longer insane. Three years later she brought an action against her nephew for having caused her detention without cause. Parkinson gave evidence for the defence, but she won the case, the nephew was sent to prison for 6 months, and Parkinson was censured by *The Times* and other newspapers. At the instigation of the College Visitors he eventually wrote his *Observations* in which he pointed out the shortcomings and deficiencies of the existing laws, and the difficulties implied in the definition of insanity. Besides criticizing the lunacy laws he put forward valuable suggestions for the improvement of reception orders and proposed measures to afford better legal protection not only to the patient, but also to keepers, physicians, and relatives. The case of Mary Daintree drew attention to the ineffectiveness of the College Commission, and there can be little doubt that Parkinson's remarks and suggestions were heeded and noted by those who later sponsored the Act of 1811.

Richard de Alarcón

1083. **Ambroise Paré**

M. MOUQUIN. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 4070–4072, Dec. 20, 1955. 2 figs.